D. H. Stansbery

CANCELLED

LIBRARY *of the*
OHIO STATE
UNIVERSITY

The Ohio State University
Columbus 10, Ohio

CANCELLED

~~QH 368
P73
Copy 14~~

COPYRIGHT, 1929, 1930,
BY
HENRY HOLT AND COMPANY, INC.

OHIO STATE
UNIVERSITY

PRINTED IN THE
UNITED STATES OF AMERICA

CONTENTS

PART I: PROTOPLASM

CHAPTER PAGE

I. Matter and Energy in Living Things . . 3

II. Structure of Living Things: the Cell and the Organism 16

III. Chemical Composition of Protoplasm and its Products 38

IV. Physico-chemical Structure of Protoplasm . 58

V. Exchanges Between the Cell and its Environment: Diffusion, Osmosis, Permeability. . 75

VI. Chemical Reactions in the Living Organism: Catalysis and Enzymes 93

PART II: NUTRITION

VII. Nutrition of the Animal Cell 107

VIII. Nutrition of the Green Plant Cell . . . 122

IX. Other Modes of Nutrition 135

X. The Food Cycle 146

XI. Nutritive Mechanisms of Multicellular Plants 156

XII. Nutritive Mechanisms of Multicellular Animals 184

PART III: RESPONSE

XIII. Stimulation and Response 236

XIV. Effectors 259

XV. Receptors 282

XVI. Coordination 293

XVII. Behavior of Organisms 333

445151 CANCELLED

PART IV: REPRODUCTION

CHAPTER PAGE
XVIII. GROWTH AND CELL DIVISION 349
XIX. REPRODUCTION OF SIMPLE ORGANISMS . . . 362
XX. REPRODUCTION OF MULTICELLULAR ANIMALS . 380
XXI. REPRODUCTION OF MULTICELLULAR PLANTS . 423
XXII. HEREDITY 452
XXIII. THE MECHANISM OF DEVELOPMENT . . . 524

PART V: EVOLUTION

XXIV. VARIATION AND SELECTION 557
XXV. NATURAL SELECTION; THE ORIGIN OF SPECIES . 590
XXVI. RESULTS OF EVOLUTION 619
XXVII. THE ORIGIN AND NATURE OF LIFE 654

APPENDIX

I. CLASSIFICATION OF ORGANISMS. 669
II. CHEMICAL SYMBOLISM AND NOMENCLATURE; CLASSIFICATION OF CHEMICAL COMPOUNDS . . 675
III. BIBLIOGRAPHY 686
INDEX 695

PREFACE

THE aim of this book is to present biology as a science—a consistent, integrated body of knowledge and theory aiming not merely to describe but to explain the phenomena with which it deals. The only unifying principle capable of serving as a basis for such a synthesis of the various fields of biological science is the concept of the living organism as a physico-chemical mechanism. Consequently the book has been explicitly and consistently built around this central concept.

This aim and this viewpoint have determined the contents and organization of the book. Its emphasis is on general principles rather than factual details, on the known rather than the unknown; the many still unanswered questions with which every phase of biology bristles are not ignored but viewed as stimulating problems rather than as discouraging mysteries.

This presentation of the subject undoubtedly makes greater demands on the ability and application of the student than a more descriptive and discursive treatment would. While no effort has been spared to present the ideas in the clearest possible form, I have not endeavored to attain simplicity at the price of superficiality. I believe the book is not more difficult than modern college textbooks of physics or chemistry, and I see no good reason why it should be less so, in view of the greater inherent complexities of the subject matter of biology.

This book was first outlined about ten years ago. For the last five years its material has been used, first as lecture notes, later as a text in photostated form, in a course of general biology given to over a thousand students each year at Washington Square College, New York University. No two teachers will probably ever entirely agree—nor will any one agree with himself in two successive years—as to the topics to be included in such a course, the relative time to be given to each, or the order of their presentation. These questions have been decided, in the present work, primarily on the basis of its fundamental aim, as stated above, modified somewhat by pedagogical considerations derived from actual teaching experience. To keep the size of the book within reasonable limits, certain whole fields of biological work have had to be omitted, though regretfully, almost entirely. The contents are still rather full for the usual eight-months college course, leaving considerable leeway to the preferences of the individual teacher in the relative emphasis to be placed on each part. I feel that there is no harm in exposing the student to more than he is expected to hand back at an examination. The organization of the book also allows some flexibility in the order of presentation of the topics.

The book is specifically planned as an integral part of a course comprising also lectures and laboratory work. For this reason very little space has been devoted to descriptions of visible structures or experimental methods, as it is felt that these can be best learned in the laboratory. The laboratory work accompanying this text may be chiefly morphological or, to a greater or less extent, experimental, depending on the preferences and facilities of the individual teacher. A laboratory manual comprising work of both these types and allowing a considerable freedom of selection, designed to accompany this text and based on actual teaching experience in the course as given here, has been prepared by Professor H. J. Fry and will be published shortly.

I take this opportunity of expressing my indebtedness to many of my colleagues in the Biology Department of New York University and to a number of biologists elsewhere for helpful suggestions in respect to the contents and organization of this book. The illustrations have all been drawn by Marie Louise Duggar (Mrs. C. R. Plunkett), who has also done much of the work of preparation of the manuscript, proof-reading, and indexing.

As is necessarily the case in any work of this kind, practically all of the facts and many of the ideas are derived from the work of others. The only respect in which any measure of originality can be claimed is in the synthesis of this material into a unified picture. In this respect the author ventures to hope that his work may be justified as a contribution to the development of the infantile—or perhaps still embryonic—science of biology.

C. R. PLUNKETT.

Department of Biology
Washington Square College
New York University
February 28, 1930.

OUTLINES OF
MODERN BIOLOGY

CHAPTER I

MATTER AND ENERGY IN LIVING THINGS

Biology is that branch of science which deals with living things. We recognize certain bodies—plants and animals—as "living," by virtue of a number of characteristic activities exhibited by them. The most obvious of these activities, usually apparent to even superficial observation, are *movement*, *responsiveness*, *nutrition*, *growth*, and *reproduction*. These activities, collectively, we call *life*, and those bodies which exhibit them we call *alive* or *living*.

These phenomena which we call life are found always, and only, associated with a particular kind of material, called *protoplasm*. Every living thing is composed, either entirely or (more usually) partly, of protoplasm. All the other materials contributing to the structure of their bodies—such as wood, bone, blood, etc.—are *produced by* the protoplasm.

Protoplasm is not a single substance, but a mixture of many substances. Some of these, such as water and mineral salts, are abundant also in non-living nature. But protoplasm is especially characterized, chemically, by containing complex substances called *organic compounds*, found nowhere in nature except as components or products of protoplasm. The most abundant (next to water) and most characteristic components of protoplasm are *proteins*, which are the most complex, chemically, of all known substances.

Along with its complex chemical composition, protoplasm has also a highly complex *structure*. The most significant features of this structure are not visible to the naked eye, but some of them are revealed by the microscope. All living things are made up of definite units, usually of microscopic size, called *cells*, which are composed of protoplasm. The simplest living things consist each of a single cell; but all the larger plants and animals, visible to the naked eye, are each composed of many cells (together with more or less non-cellular material produced by the cells). Each individual living body, whether composed of one, few, or many cells, is called an *organism*. Each cell has a complex internal structure, the most general feature of which is the differentiation of the protoplasm into two distinct parts, called *nucleus* and *cytoplasm* respectively. Within each of these parts smaller structural details can usually be seen with a good microscope. But beyond the utmost limit of microscopic visibility, protoplasm has a still finer, and probably very complex, *ultramicroscopic* structure which is revealed, to some extent at least, by indirect methods, and upon which many of its most characteristic properties undoubtedly depend.

Protoplasm is characterized by its *activities* no less than by its composition and structure. There is no such thing as "dead protoplasm": the structure and the activities of protoplasm are inseparable. For the structure of protoplasm is essentially unstable, and can only be maintained by a continuous expenditure of energy; *i.e.*, by "doing work." The source of this energy is certain chemical reactions which are always going on in protoplasm. The original source of the substances involved in these reactions is materials taken in from outside as *food*. The various processes by which food is taken into the organism, distributed to all its cells, chemically transformed within the cells, and the waste products eliminated from the body, constitute *nutrition*. The most essential phase of nutrition, the chemical processes occurring within the living cells, is called *metabolism*. A large part of the energy liberated by metabolism takes the form of *movements* of various kinds, some of which are visible to us as such, while others we recognize as heat, electric currents, and other phenomena of movement of invisibly small particles. These chemical and physical processes in the cells are influenced by many external and internal conditions—heat, light, pressure, electricity, chemical substances, etc.—and hence the activities of the organism are modified in many ways by changes in these conditions; this is called *responsiveness*. The most characteristic feature of metabolism in the living cell is the production, from some of the substances taken in as food, of more protoplasm like that already present; this process, called *assimilation*, results in *growth* of the cell and the organism. Not only is the amount of protoplasm thus increased by its own activities, but also its organized units are increased in number: cells produce new cells, and organisms new organisms, like themselves; this is *reproduction.*

We thus see that all the forms of activity which we recognize as characteristic of living things, and which constitute what we call life, are simply the characteristic and universal activities of protoplasm. *Life*, therefore, is the *activities of protoplasm*; or, conversely, protoplasm is *living matter.*

No one of these characteristic activities can be said to be absolutely peculiar to living things. A steam engine or a gasoline engine *moves* by virtue of energy derived from chemical reactions ("metabolism") of its fuel ("food") substances, and *responds*, by changes of its activities, to various changes in external and internal conditions. Crystals *grow* by selective taking up and combination ("assimilation") of suitable substances from their surroundings, not only increasing in size but also, like organisms, producing a definite form and structure. They will also, if broken, produce other crystals like themselves in composition, structure, and form; and some crystals break so readily, in certain definite planes, that they may practically be said to "reproduce" spontaneously.

It is obvious, however, that these activities of non-living things, while similar in principle to those characteristic of living things, are very much simpler. The movements, responses, chemical reactions, growth, and reproduction of living organisms are all tremendously more complex than those of any non-living systems. This difference in degree of complexity also characterizes the composition and structure of protoplasm as compared with any other material. The distinctive feature of living things is *complexity*—of composition, structure, and activities. Every complex phenomenon, however, when once it has been scientifically analyzed, is found to be simply a combination of several or many simpler phenomena, which are exhibited separately in simpler types of systems. The problem of biology is to explain the complex special phenomena of life in terms of the simpler and more general phenomena exhibited in simpler—*i.e.*, non-living—systems.

Matter and energy.—Modern science describes all phenomena in terms of two fundamental concepts: *matter* and *energy*. Matter is that which occupies space, has mass (inertia) and weight: the material, or substance, of which all things are composed. Energy is the capacity to do work; *i.e.*, to produce change, or activity. Every phenomenon—everything that happens—may be described as a change in motion or configuration of some body of matter, accompanied by a transformation or transfer of energy.

The structure of matter.—All forms of matter are made up of discrete particles, called *molecules*. A molecule may be defined as the smallest particle into which any substance can be divided and yet retain its identity; *i.e.*, remain the same substance. There are as many different kinds of molecules as there are chemically distinct substances; that is, a practically unlimited number. But all these molecules are made up of smaller particles, called *atoms*, of which there are only 92 different kinds. Each kind of molecule has a definite number, proportion, and arrangement of one or more kinds of atoms. All chemical changes—*i.e.*, processes in which one substance is changed into a different substance—consist in the disruption of molecules and the recombination of their constituent atoms into a different kind of molecules.

A substance containing only one kind of atoms is called a *chemical element*. A *chemical compound* is a substance containing only one kind of molecules, each of which consists of two or more different kinds of atoms. The elements making up a compound are said to be *chemically combined*. An *uncombined*, or *free*, element is composed of molecules containing only one kind of atoms. The term *substance* is applied to either a compound or a free element; *i.e.*, to any material composed of only one kind of molecules. Any portion of matter containing more than one kind of molecules is a *mixture* (Fig. 1). The substances (compounds or free elements) making up a mixture are called its *components*. The elements, in chemical combination, making up a compound are called its *constituents*.

The 92 different kinds of atoms are all made up, in turn, of still smaller particles, of which there are only two kinds: *protons* and *electrons*, which are particles of *positive* and *negative* electricity respectively. Each kind of atom has a definite number and configuration of these electrical particles. Every atom—and consequently also the molecules and larger bodies which they compose—normally contains an equal number of protons and electrons. Any body which has unequal numbers of these two kinds of particles is *electrically charged*: an excess of protons constitutes a *positive charge*, an excess of electrons a *negative charge*. An atom, or group of atoms—*i.e.*, a particle of atomic or molecular size—with such a charge, is called an *ion*. Two bodies (whether protons and electrons, ions, or larger bodies) with the same kind of charge repel each other, while two bodies with opposite charges attract each other; these forces are called *electrostatic* repulsion and attraction.

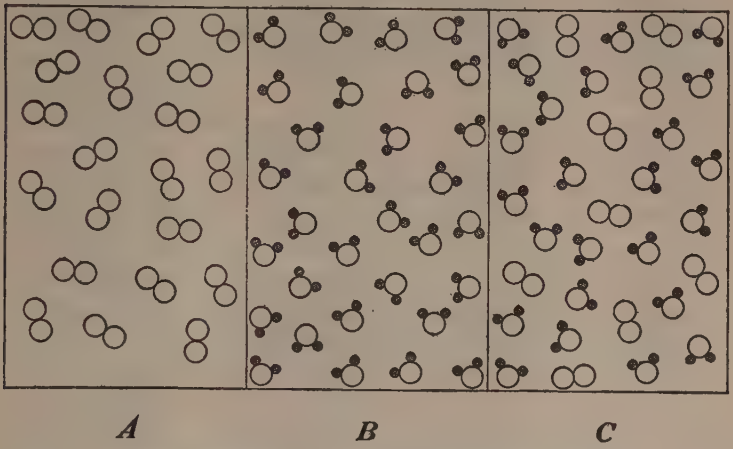


FIG. 1.—Diagrams representing composition of free element, compound, and mixture. The large open circles represent oxygen atoms, the smaller dark circles hydrogen atoms. *A*, a free element, oxygen (O_2); all the molecules are alike and contain only one kind of atoms. *B*, a compound, water (H_2O); all the molecules are alike, each consisting of one oxygen and two hydrogen atoms. *C*, a mixture of water and free oxygen, containing two kinds of molecules (H_2O and O_2), which may be mixed in any proportions.

The simplest kind of atom, the hydrogen atom, consists of a single proton with a single electron revolving about it. Every other kind of atom consists of a nucleus, containing all its protons and some (about half) of its electrons, about which the rest of its electrons (*planetary electrons*) revolve in different orbits, like the planets about the sun. Since the atom as a whole is electrically uncharged, the number of planetary electrons must be equal to the excess of protons

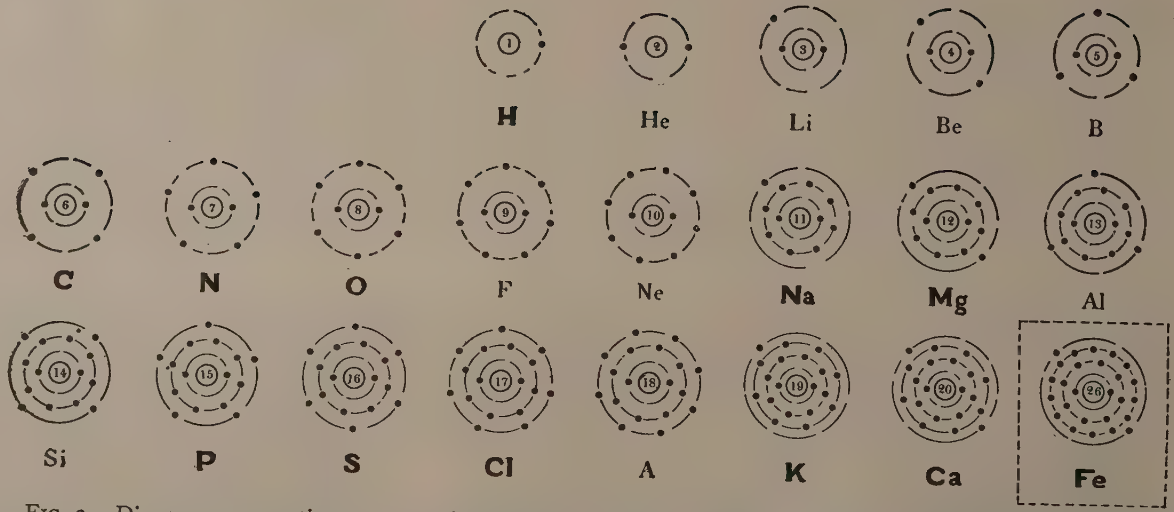


FIG. 2.—Diagrams representing structure of the atoms of atomic numbers 1–20 and 26. The central circle represents the atomic nucleus, the number in the circle showing its net positive charge, *i.e.*, the atomic number; the small black circles represent the planetary electrons. These figures are purely diagrammatic and do not pretend to show the actual spatial configurations of the electrons nor, of course, their motions. The atoms whose symbols are printed in heavy type are those of the elements generally present in living matter. **H**, hydrogen; He, helium; Li, lithium; Be, beryllium; B, boron; **C**, carbon; **N**, nitrogen; **O**, oxygen; F, fluorine, Ne, neon; **Na**, sodium; **Mg**, magnesium; Al, aluminum; Si, silicon; **P**, phosphorus; **S**, sulphur; **Cl**, chlorine; A, argon; **K**, potassium; **Ca**, calcium; **Fe**, iron.

over electrons in the nucleus. This number is called the *atomic number*, and is characteristic of each element. The nuclear charge determines the number of planetary electrons and their configuration, which, in turn, determines all the *chemical properties* of the element. Thus all atoms with the same atomic number belong to the same element, and each element has a different atomic number, from 1 (hydrogen) to 92 (uranium). In Fig. 2 are represented diagrammatically the atoms of numbers 1–20 and 26, which include all those generally present in living matter.

Certain of these electron configurations are more stable than others. Those atoms whose planetary electrons have a completely stable configuration enter into no chemical combinations at all: these are the *inert* elements (*e.g.*, He, Ne, A). Others have an unstable configuration such that they tend to lose one or more of their outermost electrons (*valence electrons*): these are the *metals*, or *electro-positive* elements (*e.g.*, those to the right of the inert elements in Fig. 2). By losing electrons, these atoms acquire a positive charge, thus becoming positive ions, or *cations*. Still other atoms have an electron configuration which is unstable in the opposite way, tending to take up one or more extra electrons, thus becoming negative ions, or *anions:* these are the *non-metals*, or *electro-negative* elements (*e.g.*, those to the left of the inert elements in Fig. 2). Many of the non-metallic elements, however, may act as either electro-negative (taking up extra electrons) or electro-positive (losing valence electrons) under different conditions (*e.g.*, H, C, N, P, S).

There are two ways in which atoms may combine to form molecules. An electro-positive atom may give up its valence electron, or electrons, to an electro-negative atom; thus the former becomes positively, the latter negatively, charged, and they hold each other by electrostatic attraction. Such molecules, composed of positive and negative ions, constitute *polar compounds*. Most inorganic ("mineral") compounds are of this type (*e.g.*, NaCl, Fig. 3). When the electrostatic force holding them together is weakened, by any means, these molecules tend to break up in such a way as to preserve stable electron configurations rather than electrical neutrality; *i.e.*, into ions rather than uncharged atoms. This occurs with many polar compounds when dissolved in other polar substances such as water, because the electrostatic attraction between the ions of the solute is weakened by the counter attractions of the polar molecules of the solvent. Substances which *dissociate* in this way, in solution, are called *electrolytes*. Their tendency to ionize varies greatly, from very *weak* (slightly dissociated) electrolytes, such as water, to very *strong* (highly dissociated) electrolytes, such as most salts.

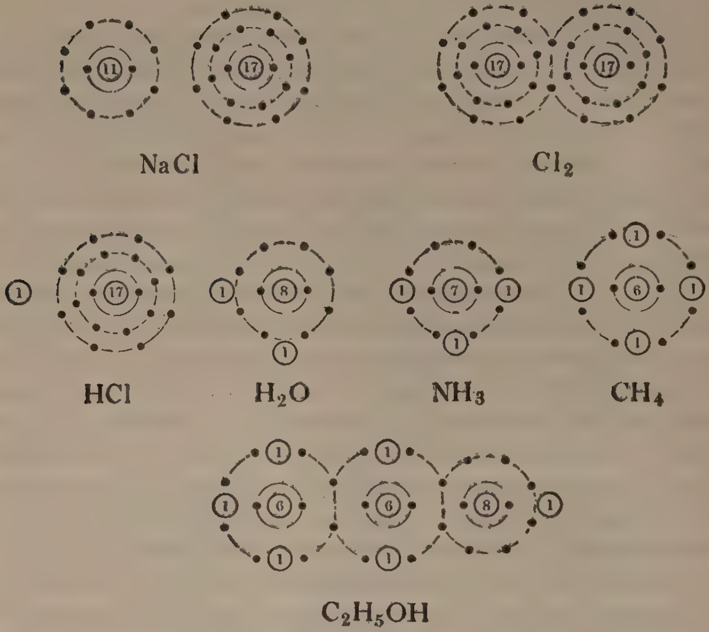


FIG. 3.—Diagrams representing structure of several types of molecules; the symbolism is the same as that of Fig. 2. NaCl, sodium chloride (common salt), a typical polar compound; Cl_2, free chlorine, a typical nonpolar molecule. Second row, a series of hydrogen compounds arranged in order of decreasing polarity: HCl, hydrogen chloride (hydrochloric acid), polar, strong electrolyte; H_2O, water, polar, weak electrolyte; NH_3, ammonia, polar, non-electrolyte; CH_4, methane, nonpolar, non-electrolyte. C_2H_5OH, ethyl alcohol, a polar-nonpolar compound; the left-hand part of the molecule (C_2H_5 radical) is nonpolar, the right-hand part (OH radical) is polar.

Two or more electro-negative atoms may combine in such a way as to mutually satisfy their need for extra electrons to produce stable configurations. Such molecules, no part of which is positively or negatively charged, constitute *nonpolar* substances. The molecules of free elements (*e.g.*, Cl_2, Fig. 3) are of this type. Some organic compounds (*e.g.*, CH_4, Fig. 3) are also nonpolar. Many other organic compounds are partly polar, partly nonpolar; *i.e.*, one part of the molecule is polar, another part nonpolar (*e.g.*, C_2H_5OH, Fig. 3). Purely nonpolar compounds do not dissociate into ions; the "mixed" type (*polar-nonpolar compounds*) may do so to a greater or less extent.

The line of separation between these two types of compounds is not sharp, since all gradations exist between the most strongly polar (electrolytic) and strictly nonpolar molecules (Fig. 3, second row). Nevertheless, the distinction is a useful one, as it has been found very helpful in explaining the chemical and physical properties of substances. In general, polar compounds react chemically very rapidly, whereas nonpolar substances react more slowly. Also, polar compounds are more soluble in other polar compounds, such as water; while nonpolar substances are more soluble in nonpolar solvents, such as oils ("like dissolves like"). In polar-nonpolar molecules, each part (*radical*) tends to behave in the way characteristic of its own type of structure, making the chemical and physical behavior of such substances often very complex. Many of the components of protoplasm are compounds of this complex type.

Matter in living things.—Living matter is a mixture of many substances; *i.e.*, many different kinds of molecules. Both in the number of its component substances and in the molecular structure of many of these substances protoplasm is far more complex than any other known mixture, natural or artificial. Like mixtures in general, and unlike pure substances, it is somewhat variable in composition. It always consists to the extent of about 99% of the four elements *carbon*, *hydrogen*, *oxygen*, and *nitrogen;* with eight others (see Fig. 2) always, or almost always, present in much smaller proportions. These twelve elements are all among those most abundant in non-living matter also. But in protoplasm these elementary constituents are combined in innumerable compounds, of many different types, some of which are much more complex (*i.e.*, contain more atoms in each molecule) than any found in non-living nature. The kinds and proportions of these components differ somewhat in different organisms and in different parts of the same organism. These compounds, moreover, are constantly undergoing chemical changes (metabolism), breaking up and recombining in multitudinous ways: so that the composition of protoplasm varies not only from organism to organism, and from cell to cell, but also from moment to moment in the same cell.

But a living thing is more than merely a mixture of many chemical substances: it is also an organized structure whose components are arranged in special physical relations. This structure of living matter, unlike that of artificial machines, is not chiefly imposed upon it from without, but results primarily from the chemical and physical properties of its own components; that is, in the final analysis, from the structure of its atoms and molecules. In and by this material structure, chemical and physical, are exhibited those activities—*i.e.*, manifestations of energy—which we call life.

Energy is manifested in various ways: as movement (of visible bodies), heat, chemical changes, electric currents, light, etc. All these manifestations of energy prove, on scientific analysis, to be *movements* of some kind of material body or particle. Thus heat is the movement of molecules; chemical change, of atoms; electric currents, of electrons. Radiant energy—light, X-rays, etc.—is transmitted through empty space, but only becomes manifest to us as it affects the movements of material particles, *e.g.*, electrons.

Besides these active manifestations of energy, material bodies may also contain energy in a form which is not apparent at the moment. Thus, a body at any distance above the ground, a stretched rubber band, an explosive mixture (*e.g.*, gunpowder), a charged electric condenser, all possess the *capacity to do work*, *i.e.*, energy. This capacity to do work is due, in each case, to the position or configuration (relative position of component parts) of the body. In general, it may be said to consist in the separation of bodies or particles which have a tendency to come together when unrestrained, due to some "attractive force," *e.g.*, gravity, cohesion, adhesion, chemical affinity, electrostatic attraction; or in the approximation of those which tend to "repel" each other, *e.g.*, by electrostatic repulsion.

Energy in its active manifestations, *i.e.*, *energy of move-*

ment, is called *kinetic energy;* energy in the (apparently) inactive forms, *i.e.*, *energy of position*, is called *potential energy*. Some of the various forms, or manifestations, of energy may be summarized as follows:

	Kinetic	*Potential*
Molar[1]	Movement (mechanical energy)	Weight (gravity)
Molecular	Heat	Cohesion and Adhesion[2]
Atomic	Chemical reaction	Chemical affinity
Electronic	Electric current	Electric charge
Radiant	Light, X-rays, etc.	

[1] Pertaining to masses of visible size.

[2] Cohesion is attraction between molecules of the same substance; adhesion is attraction between molecules of different substances.

Transformations of energy.—All these forms of energy are mutually interconvertible: *e.g.*, kinetic into potential energy, and vice versa; mechanical energy into heat; chemical into electrical energy, etc. Such changes are called *transformations of energy*. Every event (*i.e.*, everything that happens) involves some transformation of energy from one form to another, or its transference from one body (or part of a body) to another. Every such energy change involves also a change in motion or structure of some body of matter: *e.g.*, change in rate or direction of movement, in molecular state, temperature, chemical composition, electric charge, etc. The transformations of energy have been found always and everywhere to take place in accordance with two general laws. These two Laws of Energy, based on the totality of scientific experience, are regarded as the most general and fundamental of all natural laws.

The First Law of Energy is that in every transformation or transfer of energy the total *quantity* of energy remains unchanged. In any closed system (*i.e.*, one which neither loses energy to, nor gains it from, its surroundings) the total energy content remains constant, however its form or distribution within the system may change; whenever any system loses energy, some other system gains an equal amount of energy in some form, and vice versa. This law is called the *Conservation of Energy*. The proof of its exact and universal applicability in living, just as in non-living, systems is one of the foundations of modern biology.

The Second Law of Energy may be stated roughly thus: heat (*i.e.*, random molecular movement) is never entirely convertible into any other form of energy, but all other forms of energy are entirely convertible into heat. In general, in every transformation of energy a certain proportion is converted into heat (*e.g.*, friction, heating of electric wires, etc.) and thus "lost," *i.e.*, dissipated to the surroundings. Thus, although the total quantity of energy remains constant, the amount of "useful" energy always decreases. This is the law of *Degradation of Energy*.

Within the limitations of these two general laws, the transformation of energy occurring in any particular case is determined by the structure of the material system in which it occurs. If any combustible substance—*e.g.*, coal, gasoline, or sugar—be burned (*oxidized*) in an open space, its chemical energy will be transformed almost entirely into heat. To convert any considerable part of the energy of a chemical reaction into other forms—*e.g.*, mechanical or electrical energy—the reaction must occur in some organized structure, such as an engine, an electric cell, or a living organism. Thus the *activities* of any body, living or nonliving, are determined by its *structure*. Any material system which determines, by its structure, the course of the energy transformations occurring in it, may be called a "machine," or *mechanism*. In this sense, a living organism is a machine.

Energy in living things.—Practically all the forms of energy listed above are manifested in the activities of living things. *Mechanical energy* appears not only in the externally visible movements of animals, but also in the streaming movements of protoplasm within many cells, observable with the microscope, and in the slower movements involved in growth of all organisms. *Heat* is produced by all organisms, conspicuously by the "warm blooded" animals. *Chemical energy* appears in the metabolic processes which are the very essence of life. *Electrical energy* is manifested in the *bioelectric currents* which accompany every activity of the living cell; these usually require special instruments for their detection, but a few organisms (electric fishes) produce electric currents of considerable magnitude. *Radiant energy*, in the form of light, is produced by a number of organisms (*e.g.*, fireflies), though not by most.

In accordance with the law of Conservation of Energy, all these manifestations of energy by the living organism must be produced by transformation of some other form, or forms, of energy within it. The immediate source of all the energy manifested in the activities of living things is the chemical energy of certain metabolic processes, especially *oxidations*, which is derived from the chemical potential energy of certain food substances, *viz.*, organic compounds and free oxygen. Tracing the source of this energy further back, we find that these food substances of high chemical potential are produced by certain chemical reactions (*photosynthesis*) in green plants, by which the radiant energy of sunlight is absorbed and transformed into chemical potential energy of organic compounds and free oxygen. The ultimate source of all the energy of living things is, therefore, the radiant energy (light) of the sun. By far the greater portion of this solar energy, of course, is absorbed by inanimate bodies and dissipated quickly as heat. That small portion which happens to fall on the green cells of plants is also degraded eventually into heat, but by a roundabout path involving the complex series of energy transformations which constitute the activities of living things.

Life may be described, in terms of the fundamental scientific concepts, matter and energy, as a complex series of energy transformations occurring in and determined by a particular kind of complex material structure, or mechanism. This structure, at any particular time, is the result of previous activities (energy transformations) in an antecedent structure, and so on. From this point of view there is no essential difference between the phenomena of life and those of non-living nature: both consist of continuous series of energy transformations, in accordance with the fundamental Laws of Energy, and determined in detail by the particular kind of material structure in which they occur and which they in turn continuously modify. The differences between living and non-living systems are entirely differences in degree of complexity.

This scientific conception of life is summarized in the statement "*the organism is a physico-chemical mechanism*," which may be called the *fundamental postulate of modern biology*.

CHAPTER II

STRUCTURE OF LIVING THINGS: THE CELL AND THE ORGANISM

LIVING matter is never found in masses of indefinite size and form—like water, for instance—but always in the form of definitely organized bodies. The unit of protoplasmic organization, common to all living things, is the *cell*. The simpler organisms consist of single isolated cells, while the more complex ones are composed of many cells (billions in the larger organisms) differing in form and activities. The former are called *unicellular*, the latter *multicellular* organisms.

The cell.—A cell is an organized bit of protoplasm, usually consisting of two distinct regions, *nucleus* and *cytoplasm*, and usually delimited by a definite surface layer or *membrane*. To both of the last two statements there are some exceptions. The simplest organisms, *bacteria*, have no distinct nucleus and cytoplasm, but the characteristic nuclear material, *chromatin*, is distributed throughout the cell. In some of the lowest multicellular organisms, and in some tissues of higher ones, there are no limiting surfaces or membranes between the cells, but the nuclei are distributed in a continuous mass of protoplasm. Both these types of organization have been called "non-cellular," but it is more usual to regard them as variations of the universal cellular organization of protoplasm, differing from the more typical forms only in the lack of limiting membranes between nucleus and cytoplasm or between adjacent cells.

Size of cells.—The great majority of cells lie below the limit of macroscopic (naked eye) visibility, which is about 10^{-2} cm. (0.1 mm.) Most of them, however, can be easily seen with the microscope, which extends our range of vision down to about 10^{-5} cm. ($0.1\ \mu$).[1] The very smallest living organisms ("filterable viruses") are even smaller than this, probably about 3 x 10^{-6} cm. (30 mμ) in diameter; that is, of ultramicroscopic dimensions (Fig. 4, G). The smallest microscopically visible cells are *bacteria*, some of which are at the extreme lower limit of microscopic visibility (Fig. 4, F). At the other extreme of size, the largest single cells are the *egg-cells* of some fishes and birds (the egg-cell of a bird is what is popularly called the "yolk" of the egg); the egg-cell of the ostrich has a diameter of about 8 cm. Most cells, however, in both unicellular and multicellular organisms, are between 10^{-4} and 10^{-2} cm. (1–100 μ) in diameter; that is, within the range of microscopic dimensions.

---

[1] $1\ \mu$ (micron) $= 0.001$ mm. $= 10^{-4}$ cm.
$1\ \mathrm{m}\mu$ (millimicron) $= 0.001\ \mu = 10^{-7}$ cm.

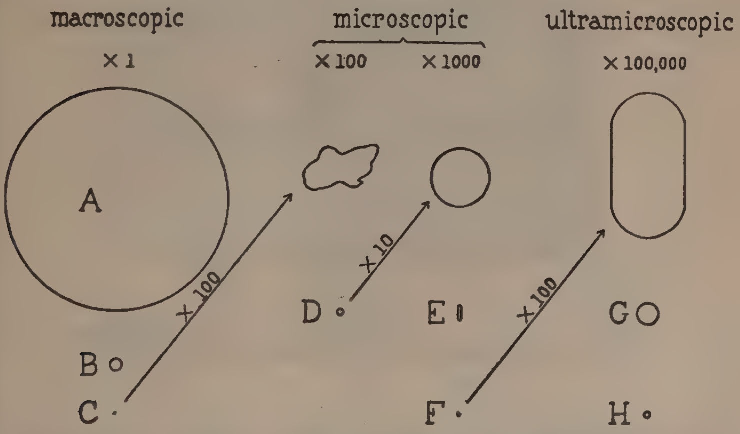


FIG. 4.—Relative sizes of cells: *A*, egg cell ("yolk") of hen's egg (3 cm.); *B*, frog's egg (1.75 mm.); *C*, Amoeba, a unicellular animal (0.1 mm. = 100 μ); *D*, red blood corpuscle of man (8.5 μ); *E*, typhoid bacillus, an average sized bacterium (2 × 0.5 μ); *F*, Bacterium pneumosintes, a probable causative organism of influenza, lying at the extreme limit of microscopic visibility (0.2 × 0.1 μ = 200 × 100 mμ); *G*, probable relative size of the "filterable virus" organism causing the mosaic disease of the tobacco plant (30 mμ); *H*, probable relative size of the largest known protein molecules (6 mμ).

External form of cells.—Isolated cells (unicellular organisms) may be spherical, elongate, flat, indefinite and changeable in shape, or of very complex but definite form. The cells of multicellular organisms may be spherical, polyhedral, flat, cylindrical, spindle shaped, stellate, complexly lobed or branched, etc. In short, different kinds of cells have almost every conceivable shape. These forms are determined partly by internal, partly by external, factors. Protoplasm is usually liquid, varying from a very fluid to a very viscous consistency; in some cells and some parts of cells it is semi-solid, jelly-like. The simplest and most typical shape of a cell is spherical, like a drop of any liquid material, but innumerable variations of this form are produced by differences of internal structure and of external forces. These non-spherical shapes may be maintained by high viscosity of the protoplasm or of its outer layer, by intracellular skeletal structures, by external rigid cell walls, or by the pressure of adjacent cells.

Internal structure of the cell.—In all but the very smallest cells there is visible, with the microscope, a complex and characteristic internal structure. Only the coarsest features of this structure are visible in the living cell, because most of the intracellular bodies are colorless or nearly so, and have nearly the same refractive index. To render them visible, they must be stained with dyes which color them differentially. Before staining, however, the cells must first be *fixed* with chemicals which solidify and preserve them, to prevent their disintegration and decay. These *fixatives* and dyes, however, may alter profoundly the original structure of the protoplasm, coagulating or precipitating its components. For this reason, we have to be very cautious in drawing conclusions as to the structure of the living protoplasm from what we see in fixed and stained preparations.

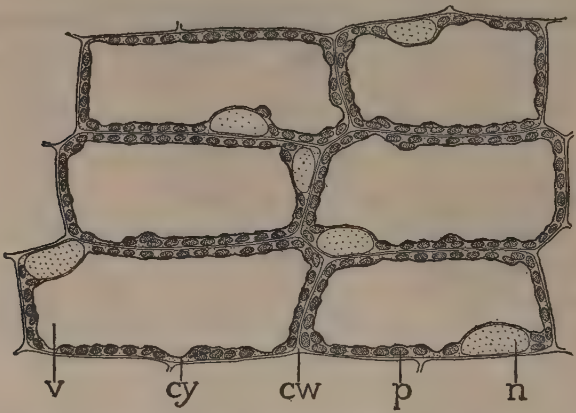


FIG. 5.—Cells of the leaf of a plant (Elodea), in the living condition. *n*, nucleus; *cy*, cytoplasm; *cw*, cell wall; *p*, plastid (chloroplast); *v*, vacuole.

In general, this kind of evidence can be accepted only when confirmed by observations on the living cell or by some kind of experimental evidence indicating the actual existence of such structures in the living state.

Every cell, in the course of its life history, passes through two visibly different stages. For the greater part of its existence as a single cell, it is in the *growth stage*, during which it may show no conspicuous structural changes; this is commonly called the "resting stage," but this term is really a misnomer, as many chemical and physical processes are proceeding actively throughout this period. At the beginning and, usually, again at the end of its individual existence, the cell appears in the *division stage*, during which it undergoes a series of conspicuous structural changes by which it is produced from half of a preceding cell and by which it gives rise to two succeeding ones (Fig. 8). This is the only way in which cells are known to be produced; namely, by division of a previously existing cell. The most striking visible differences between these two stages are in the structure of the nucleus: in the growth stage this is definitely delimited from the cytoplasm (except in bacteria) by a *nuclear membrane*, while the chromatin appears to be irregularly distributed within it; in the division stage there is usually no definitely delimited nucleus, but the chromatin is organized in definitely formed bodies, the *chromosomes*. The following description of cell structure refers, except

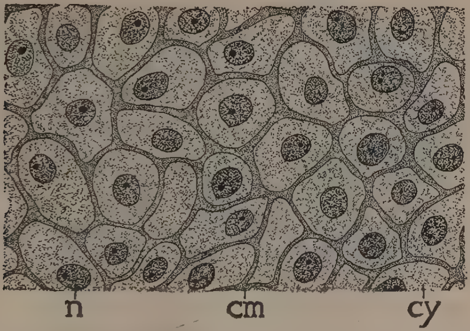


FIG. 6.—Cells of an animal tissue (from musk-gland of alligator), fixed, stained, and sectioned. *n*, nucleus; *cy*, cytoplasm; *cm*, cell membrane or intercellular substance.

where otherwise specified, to the growth stage ("resting stage").

The most general feature of intracellular structure in most cells (except bacteria) is the division of the protoplasm into *nucleus* and *cytoplasm*. Besides this, there are usually other differentiated regions or *formed bodies* within the cytoplasm; and *membranes*, of various kinds, about and within the cell.

The nucleus is usually a rounded (more or less spherical) transparent body lying near the center of the cell; but there are considerable variations, in different kinds of cells, in both its form and its position. Its relative size also varies from almost the whole volume of the cell to a very small fraction of it; but the ratio of nuclear to cytoplasmic volume is fairly constant for any one kind of cells. The consistency of the nucleus, like that of protoplasm in general, may be very liquid or quite solid (jelly-like), and may vary at different stages in the same cell.

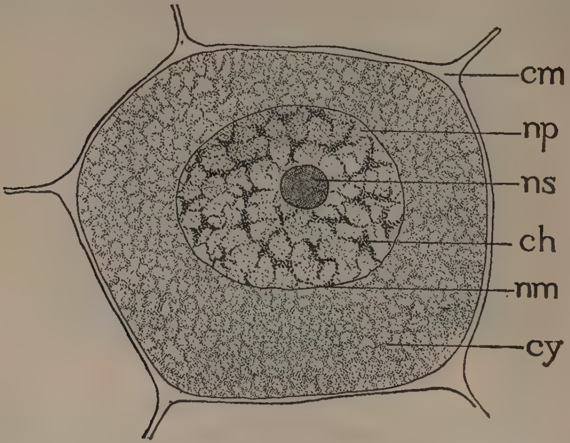


FIG. 7.—A cell similar to those of Fig. 6, more highly magnified. *ch*, chromatin; *np*, nucleoplasm or nuclear sap; *ns*, nucleolus; *nm*, nuclear membrane; *cy*, cytoplasm; *cm*, cell membrane.

The nucleus consists of a ground substance called *nuclear sap* or *nucleoplasm*, and the *chromatin*. The ground substance is not conspicuously different in any way from that of the cytoplasm, described below. The chromatin, which is the distinctive component of the nucleus, is usually not separately visible in the living cell in the growth stage, but can be made visible by staining. After the cell has been killed, fixed, and stained, the chromatin appears as a network or as scattered granules distributed through the nucleoplasm; but this is probably not a reliable indication of its distribution or structure in the living state.

At the beginning of the division stage, the chromatin becomes aggregated into threads, which later contract into short rods, of definite number, size, and shape, the *chromosomes* (Fig. 8). These are visible, under proper conditions, in the living cell, and retain essentially the same form in the fixed preparations; they stain even more intensely with certain dyes than the chromatin of the growth stage. The number, size, shape, and to some extent the arrangement, of the chromosomes is identical in all the dividing cells of all individuals of any one species of organisms (Chapters XVIII–XXII). It has been proved, further, by the study of the phenomena of heredity (Chapter XXII), that each chromosome is made up of a large number of qualitatively different substances or particles, arranged in a linear order (*i.e.*, in a "string"). These structural units of chromatin, the *genes*, are responsible for all the hereditary characteristics transmitted from cell to cell and from parent to offspring. Each gene grows and reproduces itself (*i.e.*, divides into two identical genes) between each two successive cell divisions. The genes are the essential agents of assimila-

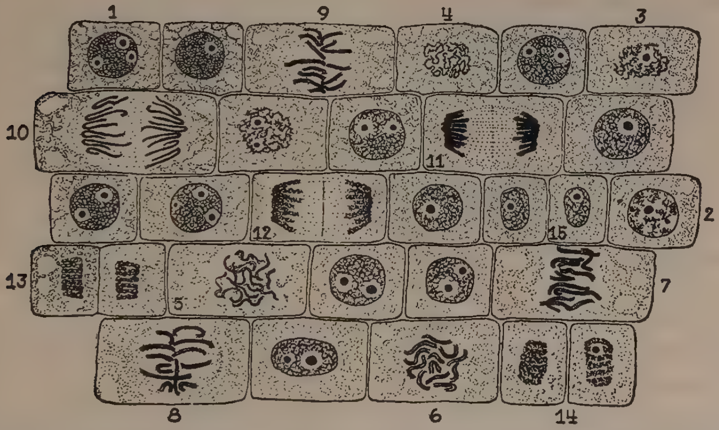


FIG. 8.—Portion of section of root-tip of onion, fixed and stained. *1*, cell in growth or "resting" stage; *2–14*, successive stages of cell division; *15*, cells shortly after completion of cell division.

tion, growth, and reproduction, and probably, in the final analysis, of all the phenomena of life. The individual genes are below the limit of microscopic visibility, being not more than 6×10^{-6} cm. in diameter; *i.e.*, of ultramicroscopic dimensions. The evidence from the study of heredity, however, proves conclusively that they retain their grouping and linear arrangement in the chromosomes through successive cell generations. The chromosomes must therefore maintain their individuality and essential structure throughout the growth stage, even though they cannot be seen at this stage in either the living or the fixed cells.

There are in many, though not all, nuclei one or more small rounded bodies called *nucleoli*. These usually disintegrate and disappear in the division stage. Their functions are unknown; they may be merely waste substances.

Certain kinds of unicellular organisms have regularly two nuclei: one of these is the true nucleus, with the persistent nuclear organization described above, while the other is a more temporary body of nuclear material (chromatin) which disintegrates and disappears at certain stages of the life history of these organisms. There are also, both as whole organisms and as tissues of higher forms, continuous masses of protoplasm containing many nuclei. These are sometimes called "multinucleate cells," but it is better to regard them as multicellular organisms or tissues without limiting membranes between the individual cells; such a tissue is called a *syncytium*.

In the *bacteria* and some other very simple unicellular organisms, there is no division into nucleus and cytoplasm at any stage; the chromatin appears to be distributed throughout the cell in small particles called *chromidia*. In some cases, at least, these chromidia appear to be organized into definite chromosomes at the division stage; whether this chromosomal organization is really persistent throughout the growth stage, as in higher organisms, is not yet known. Such organisms may be regarded as nuclei without cytoplasm, or as cells with "scattered nuclei." In certain groups of unicellular plants, related to the bacteria, all gradations exist between such scattered nuclei and typical, definitely delimited nuclei.

The nucleus, or nuclear material (chromatin), is essential for all the *constructive* activities of the cell: synthetic chemical processes, assimilation and growth. Certain unicellular organisms can be cut into pieces, some of which contain the nucleus or parts of it, while other pieces are without nuclear material. The non-nucleate fragments may move, respond, carry on oxidation and other *destructive* metabolic processes for some time; but they cannot grow, reproduce, or restore the form of the whole cell or produce cell walls or shells. They cannot even digest food, because of the lack of *enzymes* (Chapter VI), substances which are synthesized by the cell and are necessary for digestion. These fragments therefore diminish in size, by using up their own substance, and eventually die. The fragments containing a nucleus or part of a nucleus, on the other hand, even though they may be only small fractions of the original cell, can grow, restore the original size, form, and structure of the whole cell, and become perfectly normal organisms again. In many cells in which growth or the production of special structures (*e.g.*, cell walls) is proceeding most rapidly at one point, the nucleus lies close to this point (Fig. 9). In certain kinds of cells (*e.g.*, gland cells) in which synthetic chemical processes are especially active, the nucleus is very large and complexly lobed or branched, *i.e.*, has a very extensive surface (Fig. 9, D). All these facts point to the essential rôle of the nucleus

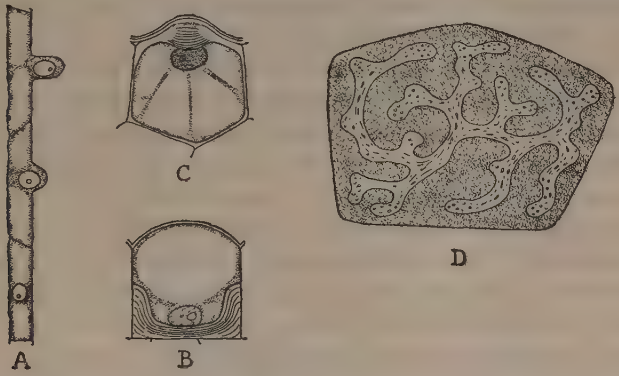


FIG. 9.—*A*, growth of root-hairs from epidermal cells of root of plant; note the location of the nuclei close to the points of rapid growth. *B*, *C*, plant cells forming local thickenings of the cell walls, with the nucleus close to the point of special thickening in each case. *D*, a cell of the silk-gland of a caterpillar, with a large branching nucleus. (*A*, *B*, and *C* after Haberlandt, *D* after Korschelt.)

in the constructive, *i.e.*, synthetic, metabolic processes of the cell. In a later chapter (Chapter XXII) evidence will be presented which shows that the actual agents in these nuclear activities are the individual genes composing the chromosomes.

The cytoplasm consists of a general ground substance containing various kinds of formed bodies. The ground substance is what we usually have in mind when speaking of "cytoplasm." The microscopic appearance of the living cytoplasm may be quite clear and homogeneous, granular, or emulsoidal. In fixed preparations, it often appears to have a reticular (network-like) or alveolar (honeycomb-like) structure; this varies according to the particular fixative employed, as well as the kind and state of the cell, being produced by the coagulation and precipitation of the protoplasmic components by the chemicals in the fixatives. The consistency of the cytoplasmic ground substance varies from fluid to solid, and may change quite suddenly in the living cell, as shown by the cessation and resumption of Brownian movement (p. 62) and of streaming movements of the cytoplasm. In some cells, the cytoplasm is differentiated into two parts: an outer, clear, more solid layer (*ectoplasm*), and an inner, granular, more fluid portion (*endoplasm*). In most types of cells, the cytoplasm fills most or all of the space between the nucleus and the outer boundary of the cell; but in the older cells of many plants, it is confined to a layer immediately inside the cell wall, the rest of the space being occupied by a large *vacuole*; the nucleus may lie in the peripheral layer of cytoplasm or in the center of the cell, connected with the peripheral layer by narrow strands of cytoplasm (Figs. 5, 14).

The cytoplasm seems, in many cases at least, to be the seat of the *functional metabolism* of the cell, as distinguished from the *constructive metabolism* of assimilation and growth. By functional metabolism is meant the destructive chemical processes (oxidation, etc.) by which energy is released in the forms of movement, heat, electric currents, etc. Many cells can perform their characteristic physical activities, involving, of course, energy-releasing chemical reactions, for some time in the absence of a nucleus; but such enucleate cells always die eventually because of their inability to synthesize the substances necessary for their own growth and repair. The cytoplasm also serves as a medium of exchange of food and waste substances between the nucleus and the outside environment; these substances, however, may undergo many and complex chemical changes in passing through the cytoplasmic zone.

Formed bodies.—In practically every kind of cell large enough for its internal structure to be microscopically visible, there are various kinds of differentiated regions or structures within the cytoplasm; these are called, in general, *formed bodies*. They are very diverse in composition, structure, and activities. Some of them are very active metabolically, others more inert, but there is no sharp line of distinction between these. We shall mention here only some of the most generally occurring types of microscopically visible formed bodies, beginning with those of greatest metabolic activity.

Plastids are definite and persistent bodies, found especially in plant cells, which are the seat of special chemical processes of a synthetic nature. They are usually spherical or oval in form, though various other shapes occur. In many, though apparently not in all, cases they grow and divide, and may even be transmitted from parent to offspring independently of the nuclear genes (p. 509). The best known plastids are the green *chloroplasts* found in all green plant cells, which synthesize carbohydrates from inorganic substances (Fig. 5). Other, usually smaller, plastids synthesize starch (from sugars), fats, pigments, etc.

Chondriosomes and *Golgi bodies* are bodies of more indefinite and changeable form than plastids. They are found in many kinds of cells, both plant and animal. It is by no means certain that all the bodies designated by each of these names are similar in composition, origin, or function, or even really present as such in the living cell. Their recognition depends on their susceptibility to certain stains; some of them may be coagulation or precipitation products of the fixatives employed. Their functions are not definitely known, but it seems probable that some of them, at least, may be, like plastids, the seat of special chemical processes of a synthetic nature. In some cases, plastids seem to originate from granules which look like small chondriosomes.

Fibrils (small fibers or threads) of various kinds occur in many cells. Many of the fibrils seen in fixed cells are probably coagulation products; but in some kinds of cells they are undoubtedly really present in the living state. The longitudinal fibrils of *muscle cells* play an essential rôle in the activity (contraction) of these cells (Chapter XIV). Characteristic fibrils also appear in nerve cells, gland cells, epithelial cells, etc., at least in fixed preparations; but the functions of these are unknown, and it is not entirely certain that they are present as such in the living cells. Besides these permanent fibrils, structures resembling fibrils appear in all cells in the division stage (Chapter XVIII).

Granules of more or less inert materials are found in practically all cells. Many of them are *stored food granules:* starch grains (in plant cells), fat droplets, yolk granules (in egg cells), etc. Others are *secretory granules; i.e.*, substances produced by synthetic processes of the cell, which are later dissolved and secreted to the outside (Chapter XIV). Some are *pigment granules*, which give characteristic colors to the cells and tissues containing them. Many of these granules are probably purely waste products or useless substances; *e.g.*, crystals of insoluble salts, unoxidizable organic compounds, etc. The size of these granules extends down to the limit of microscopic visibility and beyond, grading insensibly into the ultramicroscopic particles universally present in protoplasm. In the ultramicroscopic, and even in the extreme microscopic, region it is impossible to distinguish between "inert" particles and the essential components of protoplasm.

Vacuoles are droplets of liquid (*cell sap*) within the cytoplasm, found especially in plant cells. In the older cells of most plants, a single large vacuole occupies most of the space within the cell, surrounded by a relatively thin layer of cytoplasm. The cell sap within the vacuoles is chiefly water, with various dissolved substances, such as salts, sugars, etc. The contents of the vacuole may be regarded as inert matter, but the vacuole is always surrounded by a membrane which is part of the living protoplasm. Vacuoles have various functions. The large vacuole of plant cells maintains the rigidity (*turgor*) of the cell (Chapter V). Many unicellular animals have regularly pulsating vacuoles (*contractile vacuoles*), which excrete excess water (Chapter VII). Unicellular animals, and some multicellular ones, also form temporary vacuoles in which their food is digested (Chapters VII, XII).

Cell membranes.—At every surface of contact of protoplasm with any other material (external water or body fluids, cell sap in vacuoles, etc.) there exists a surface film which is denser, and different in other respects, than the body of the protoplasm. The film of this nature bounding the cytoplasm externally is called the *plasma membrane.* The plasma membrane has a rather tough consistency and serves to sharply delimit the protoplasm and prevent its mixing with the surrounding fluids. It also limits and controls the passage of dissolved substances into and out of the cell (Chapter V). This membrane, being not more than a few molecules in thickness, is not microscopically visible as a separate structure but merely as the boundary line of the protoplasm. The plasma membrane is an integral part of the living protoplasm, and is just as much alive as any other part of it. It should not be confused with the external, secreted cell walls and cell membranes described below; nor, on the other hand, with the ectoplasm (visible outer layer) of some cells (Fig. 11). Whenever a cell is cut or its surface ruptured, a plasma membrane quickly forms on the free protoplasmic surface.

A membrane essentially similar to the external plasma membrane surrounds every vacuole within the cell. A somewhat similar membrane separates nucleus and cytoplasm; this *nuclear membrane* is usually even tougher and less permeable than the external plasma membrane.

Outside the protoplasmic surface film, or plasma membrane, which is always present, most kinds of cells have a cell wall or membrane which is not strictly a part of the protoplasm, but is produced by it. These external nonliving membranes may be produced by secretion (*i.e.*, formed of substances synthesized in the protoplasm and poured out upon its external surface) or by chemical transformation of the external layer of the protoplasm, which then forms a new surface film (plasma membrane) within this. Almost all plant cells are surrounded by a relatively thick, rigid *cell wall*, composed chiefly of *cellulose*, a very insoluble and chemically inert carbohydrate (p. 46). Some animal cells—*e.g.*, Amoeba (Fig. 11)—are "naked," *i.e.*, have no membrane outside the plasma membrane; but most animal cells are surrounded by a thin, flexible external membrane, or *pellicle*.

Some unicellular organisms form *shells* of organic or mineral substances; others secrete thick gelatinous envelopes. Many cells of multicellular animals secrete *intercellular substances* of various kinds. There is really no sharp distinction between "cell membranes" and "intercellular substances"; the latter term is more usually employed when the material between the cells is relatively thick. In some tissues the volume of intercellular substance may finally greatly exceed that of the cells, which then lie widely separated in a mass of non-living material (bone, cartilage, etc.).

Organisms may be *unicellular* or *multicellular*. In the former each cell is an individual organism; in the latter the individual is made up of many cells. The line of demarcation between these two groups of organisms is, however, by no means sharp; there are many borderline forms in which it is difficult to say what should be regarded as an "individual."

Within each of these groups there are great differences in degree of structural complexity.

Ultramicroscopic organisms.—The smallest and presumably simplest living organisms are invisible with even the highest powers of the microscope and pass through filters whose pores are known to be of ultramicroscopic dimensions. These *filterable viruses* are known by their effects: they cause certain specific diseases in larger organisms, including animals, plants, and even bacteria. They are considered living organisms because they have the power of growth and reproduction, and certain of their effects indicate that they are composed of proteins. The pathogenic effects by which they are detected are results of their metabolic processes. Whether there are any ultramicroscopic organisms living outside and independently of larger organisms is not yet definitely known, but there is some indication that there are.

The size of these ultramicroscopic organisms can be roughly estimated by studying their ability to pass through filters of varying fineness. The probable size of some of them is thus found to be about 3×10^{-6} cm. ($30\ m\mu$) in diameter. This is not a great deal larger than the probable size of the largest known protein molecules, which may be as great as 6×10^{-7} cm. ($6\ m\mu$) in diameter (Fig. 4). These smallest and simplest of living things may therefore consist of not more than a few molecules of protein, and can hardly be supposed to have any very complex structure over and above the chemical structure of these molecules; but they exhibit the characteristic life phenomena of metabolism, growth, and reproduction. They may probably be regarded as comparable to the ultramicroscopic *genes* which are the most essential components of all living cells.

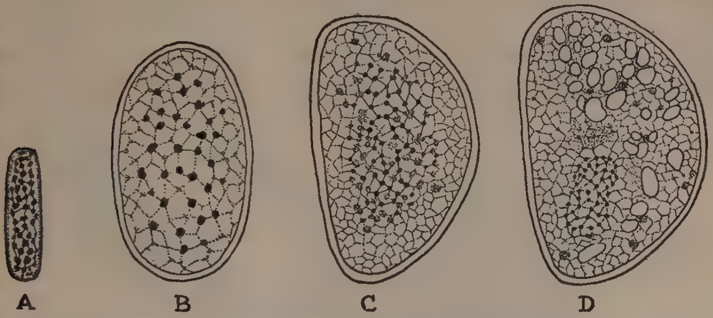


FIG. 10.—Simple organisms with "chromidial" nuclei; the most darkly stained material is the chromatin. *A*, a typical bacterium, with the chromatin distributed throughout the cell. *B*, *C*, and *D*, different species of Cyanophyceae, showing conditions intermediate between the distributed and the definitely delimited types of nuclei. (*B*, *C*, and *D* after Acton.)

Bacteria are the smallest and structurally simplest visible organisms. The smallest of these, lying at the very limit of microscopic visibility, appear as mere specks with the highest powers of the microscope, and therefore have no visible internal structure. They stain like *chromatin*, and chemical analysis also indicates that they consist largely of this material. The larger bacteria—those large enough to have any visible internal structure—consist of chromatin distributed through a non-chromatinic ground substance; that is, they have somewhat the structure of the nuclei of more complex cells. They are usually surrounded by external cell walls, similar to those of typical plant cells, and often by gelatinous extracellular envelopes; many kinds also have *flagella* (Fig. 37). But they lack the most characteristic structural feature of most cells: the differentiation between nucleus and cytoplasm. These bacteria may be regarded either as nuclei without cytoplasm or as cells with the nuclear material distributed through the cytoplasm.

This distributed, or *chromidial*, type of nucleus, is also found in some other simple organisms, especially in the *Cyanophyceae* (blue-green algae). In this group, which is regarded as related to the bacteria, are found various conditions intermediate between the distributed type of nucleus and the typical nucleus-cytoplasm structure of most cells (Fig. 10).

Other unicellular organisms have nucleus and cytoplasm sharply delimited by a nuclear membrane, at least in the growth ("resting") stage. There are a great many kinds of these unicellular organisms. Some of them are *plant* cells, others are *animal* cells, this distinction being based primarily on their mode of nutrition (Chapters VII, VIII). But the line of demarcation between these two groups is not at all sharp, for many of these simple organisms are intermediate between, or combine some of the characteristics of, plants and animals (Chapter IX). The most general structural difference between plant and animal cells is the possession by the former of a rigid external *cell wall* composed chiefly of *cellulose* or similar substances (for this

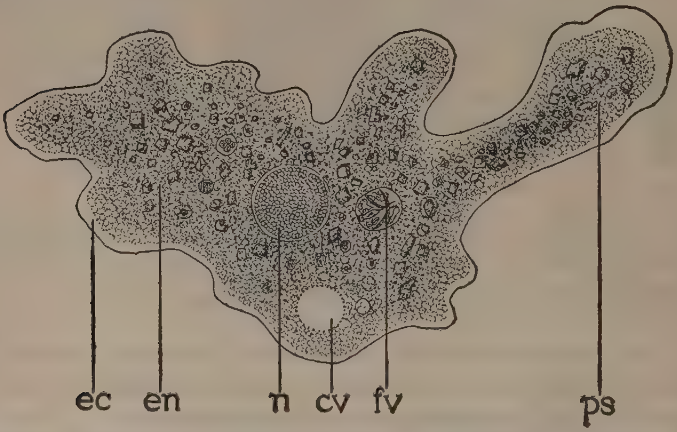


FIG. 11.—Amoeba, a unicellular animal, *n*, nucleus; *en*, endoplasm; *ec*, ectoplasm; *cv*, contractile vacuole; *fv*, food vacuole; *ps*, pseudopodium.

reason the bacteria are commonly classed as plants). Plants also usually contain *chlorophyl*, a green pigment, though there is one large group (the *fungi*) which do not. *Motility* (in the sense of external movement, or locomotion) is more usual among the animal forms, but there are many exceptions to this rule both ways.

Those unicellular organisms which are regarded as animals are called *protozoa;* the plant forms containing chlorophyl are called *algae*, and those without chlorophyl *fungi*. These terms are not confined to strictly unicellular forms, but also include some other simple types of organization, as explained below.

Among the typical unicellular organisms, with distinct nucleus and cytoplasm, there are great differences in degree of intracellular differentiation, especially in the cytoplasm. This is often differentiated into ectoplasm and endoplasm, and into various "cell organs," such as plastids, contractile vacuoles, cilia, flagella, cell walls and membranes, etc. (Figs. 11, 12). The greatest complexity of unicellular organization is attained by the ciliate protozoa, such as Paramecium (Fig. 27). In these, not only is the cytoplasm differentiated into many quite complex structures, but also the nucleus is divided into two parts (*macronucleus* and *micronucleus*) probably having different functions, a condition found in no other cells. Intracellular differentiation reaches its highest development in these protozoa. In multicellular organisms, specialization of parts is chiefly among different cells, rather than within the individual cell.

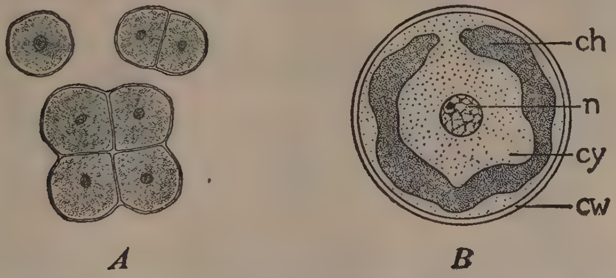


FIG. 12.—Pleurococcus, a unicellular green plant. *A*, temporary aggregates of cells, as they occur naturally. *B*, a single cell, more highly magnified, stained and sectioned. *n*, nucleus; *cy*, cytoplasm; *ch*, chloroplast; *cw*, cell wall.

Syncytial organisms.—Among the lower organisms (protozoa, algae, fungi, etc.), there are some forms which consist of continuous masses of protoplasm with many nuclei. These are sometimes called "multinucleate cells"; but as the nucleus is certainly a more essential feature of cell organization than a cell membrane, it seems better to count each nucleus with its surrounding cytoplasm as one cell. Such an organism, in which there are no limiting membranes between the individual cells, is called a *syncytium.*

One group of syncytial organisms are the slime molds (Fig. 13). Each of these consists of a naked mass of protoplasm, sometimes as much as a foot in diameter, called a *plasmodium.* They resemble giant amoebae with many nuclei. The plasmodia have no "individuality": one plasmodium may separate into two or more, or several plasmodia may coalesce into one. Under certain conditions, the whole plasmodium divides into separate cells, each containing a single nucleus and surrounded by a cellulose cell wall. From these *spores* come uninucleate amoeboid cells, which eventually coalesce to form a plasmodium again.

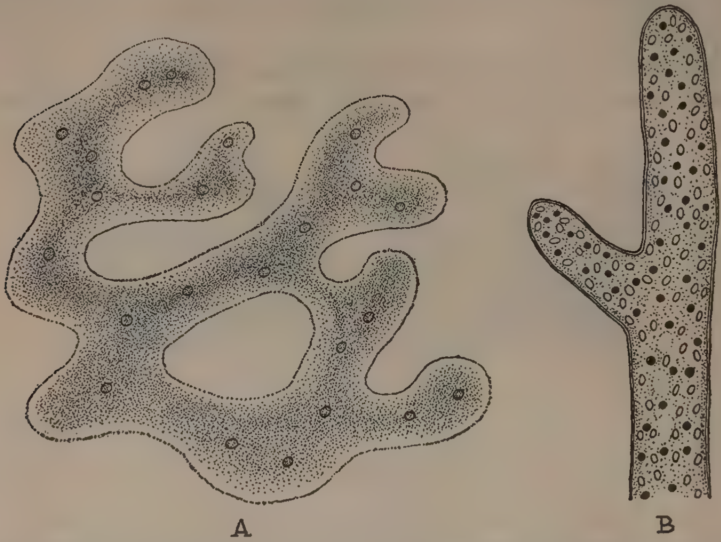


FIG. 13.—Syncytial organisms. *A*, small plasmodium of a slime mold, with many nuclei scattered through the continuous mass of cytoplasm. *B*, small portion of filament of Vaucheria, a syncytial green alga, with many nuclei and chloroplasts scattered through the continuous cytoplasm.

There are also certain green algae which are syncytial, the whole organism consisting of a long, branched filament with many nuclei and chloroplasts scattered throughout the protoplasm (Fig. 13). Many fungi (*e.g.*, the common molds) are also syncytial, resembling the syncytial filamentous algae except that they lack chloroplasts. Some other algae and fungi are semi-syncytial; *i.e.*, they consist of large "cells" each of which is really a syncytium with several or many nuclei.

Syncytia, or "multinucleate cells," also occur as component parts of some higher organisms. But the usual type of organization among higher organisms is that of uninucleate cells separated by cell walls or intercellular membranes.

Colonial organisms.—In most protozoa, the two cells formed by each cell division usually swim or crawl away from each other and form completely separate individuals. Thus most (though not all) of the species in this group are strictly unicellular. But in many algae, fungi, and bacteria, the cells, having no means of locomotion, remain attached temporarily or permanently. In these groups, therefore, strictly unicellular species are the exception; most of them are *colonial*. In some cases—*e.g.*, Pleurococcus (Fig. 12), yeast, and many bacteria—the colonies are only temporary and of no definite size or form; they are readily broken up by any mechanical disturbance. Most algae and fungi, however, form permanent colonies of very definite and characteristic forms. Such colonies are also formed by some

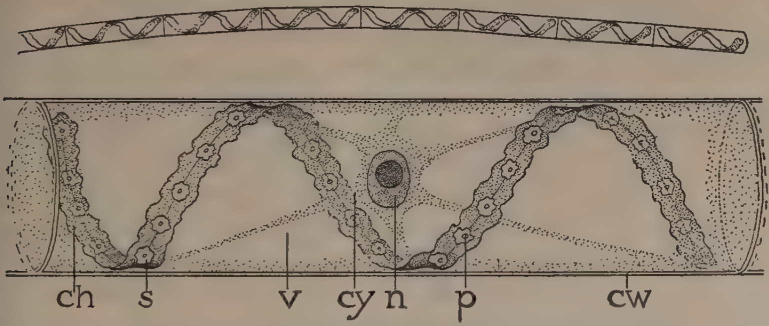


FIG. 14.—Spirogyra, a simple colonial green alga. Above, a small portion of a filament, showing the arrangement of the cells. Below, a single cell more highly magnified. *n*, nucleus; *cy*, cytoplasm; *ch*, chloroplast; *p*, pyrenoid body; *s*, starch grains; *v*, vacuole; *cw*, cell wall.

species of protozoa. These colonies are of many different forms, depending on the direction of growth of the cells and of the planes of successive cell divisions. Some are *linear* (filamentous): either straight, as in Spirogyra (Fig. 14) and some other algae, some bacteria (Fig. 37) etc.; or branched, as in many algae and fungi and some protozoa. Other colonies are *flat:* in some cases quite simple, consisting of but a few cells in one layer; in other cases, as in the larger algae (seaweeds), much more complex, having several or many layers of cells, often complexly branched and resembling in superficial appearance the forms of higher plants. Some kinds of free swimming algae form *spherical* colonies; the simpler ones are solid spheres of but a few cells; the more complex ones are hollow spheres composed of thousands of cells.

Multicellular organisms.—Just as it is impossible to draw a sharp line between unicellular and colonial organisms—because plants like Pleurococcus, yeast, etc., may exist in either form—it is equally impossible to draw a sharp line between colonial and multicellular organisms. In a colonial organism all the cells are alike and essentially independent of each other. Such a condition is seen, for instance, in Spirogyra. But in many colonial algae, some of the cells are slightly different from the others, and these colonial forms pass, by insensible gradations, into differentiated multicellular plants (Chapter XI).

The characteristic feature of a *multicellular organism*—as distinguished from a colony of cells—is that its component cells differ from each other, both in *structure* and in *function*, and are mutually dependent. In all the more complex multicellular plants and animals, the various kinds of cells are grouped into *tissues*. Each tissue consists of one kind of cells, and often contains also more or less *intercellular* material produced by its cells. There are many kinds of tissues, differing in the nature and the arrangement of their component cells and in the nature and amount of their intercellular materials. In some tissues there is very little intercellular material—merely thin membranes separating the cells—while in others the volume of intercellular material greatly exceeds that of the cells themselves. The former are usually the more active types of tissues, while the latter have more passive functions such as support or protection.

The tissues, in turn, are grouped into *organs*, each organ usually containing several kinds of tissues. An organ is a localized part of an organism, performing some particular function. All those organs which together perform some more general function are called a *system of organs; e.g.*, the digestive system, the nervous system, etc. All the organs may be classified, according to their functions, into three general groups: organs of *nutrition*, organs of *response*, and organs of *reproduction*. The various types of organs which subserve these general life functions in different kinds of organisms will be discussed in later parts of this book (Parts II, III, and IV).

Interrelations of cells in the multicellular organism.—The cells of a multicellular organism are functionally connected and their activities correlated in several ways. In some tissues the adjacent cells are connected by fine strands of protoplasm (*protoplasmic bridges*) which penetrate the intercellular membranes. Even in the absence of such protoplasmic connections many substances can pass from cell to cell by *diffusion* through the cell walls and membranes (Chapter V). In the higher plants and animals distribution of foods and other substances among the cells is effected chiefly by the *body fluids* (sap, blood, lymph, etc.) which bathe all the cells. Another kind of connection among the cells is effected by the *nervous system* in animals. The blood vessels may be compared to pipes which transmit *substances*, the nerves to electric wires which transmit a form of *activity*.

By these means, all the cells of the multicellular body are enabled to act together as a unified whole—the *organism*. Whatever the organism does is done by its cells; the non-cellular parts of the organism are lifeless products and passive tools of the living cells. The *life* of the organism is the life of its component cells. It is sometimes said that "the organism is something more than the sum of its component cells." It might be said, in the same sense, that the cell is something more than the sum of its component substances. But these mean no more than the similar statement that an engine is something more than the sum of its component parts. In all these cases, the properties of the whole are determined by the relations, as well as by the natures, of its parts. The activities of an engine, a cell, or a multicellular organism are the result of interaction, rather than independent action, of its component parts.

Classification of organisms.—Among the many different kinds of organisms there are various degrees of resemblance and difference, according to which they are *classified* into groups and sub-groups of various magnitudes. The system of classification attempts to coincide with the natural relations among organisms—*i.e.*, their presumed relations by descent—so far as possible, but the primary object of classification is convenience, and any classification of natural objects is necessarily largely arbitrary since natural objects and phenomena simply do not come in neatly defined parcels for our convenience. The lines of demarcation between groups are often ill defined, as there are many borderline forms which might be placed with equal justification in one group or another.

The primary division of organisms is into two *kingdoms: plants* and *animals*. The dividing line between these two groups is not at all sharp, as we have already seen, for there are many simple organisms which have some plant and some animal characteristics. Purely as a matter of convenience these are placed in one kingdom or the other; thus bacteria and fungi are classed as plants, although they have no chlorophyl, and the *flagellates* are commonly classed as animals although many of them do have chlorophyl (Chapter IX).

Each kingdom is divided into several large groups called *phyla*. The phylum *Schizophyta* includes the bacteria and Cyanophyceae, very simple organisms without distinctly delimited nucleus and cytoplasm. The phylum *Thallophyta* includes the unicellular, colonial, and simplest multicellular plants (algae and fungi) with distinct nucleus and cytoplasm. The phylum *Protozoa* comprises the unicellular and colonial animals. All the remaining phyla of both kingdoms consist of multicellular organisms with well-marked differentiation among their component cells.

These large groups are further subdivided into smaller ones, and so on. The generally recognized categories are, in descending order of magnitude: *kingdom*, *phylum*, *class*, *order*, *family*, *genus*, and *species*. Other ranks are sometimes interpolated between these, as subkingdom, subphylum, subclass, etc.

The term *species* corresponds to what is popularly called one "kind" of organism; generally speaking, a species may be said to consist of individuals all of which interbreed freely under natural conditions. No very exact definition, however, can be given of this or any of the other categories of classification; they are all essentially arbitrary groups.

Almost a million species of organisms have been described and named, and there are undoubtedly many others which have not yet been. Each species is designated by a *binomial* name, composed of the *generic* name followed by the *specific* name; *e.g.*, *Homo sapiens*. In the case of organisms which have no common English names, we often employ the generic name alone when, as is often the case, we are not concerned especially with any one species in particular; such names as *Amoeba*, *Paramecium*, *Spirogyra*, etc., are generic names used in this way.

The classification of organisms into phyla and classes is given in an appendix at the end of this book for convenience of reference.

CHAPTER III

CHEMICAL COMPOSITION OF PROTOPLASM AND ITS PRODUCTS[1]

PROTOPLASM, as already noted, is a mixture of many substances. One of the characteristics of a mixture, as distinguished from a pure substance, is that it is more or less variable in composition; *i.e.*, no two samples are exactly alike in the kinds and proportions of their components. We can therefore only speak of an *average* composition.

Most organisms, especially the more complex ones, contain more or less lifeless material—*e.g.*, bone, shells, wood, etc.—in addition to the actually living cells. The composition of these lifeless parts differs much more, in different kinds of organisms, than that of the protoplasm itself. Even within the cells, there are often visible bodies which are obviously lifeless: starch grains, crystals, etc. (p. 26). Aside from these, it is a difficult matter to decide which of the numerous substances in the cell are integral components of the living protoplasm and which are food and waste materials, *i.e.*, substances which have not yet entered, or have already passed through, the complex of chemical reactions which constitutes life. Since the distinctive properties and activities of protoplasm are common to all living cells, it seems reasonable to regard as its essential components those substances which are found in all cells.

Chemical analysis of many kinds of cells from various plants and animals shows a certain few elements, and certain general classes of compounds, always present. The exact proportions of these and the specific compounds (within these general classes) vary, however, in different organisms and different kinds of cells. These same elements and classes of compounds are found in the lifeless products of protoplasm, such as reserve food substances synthesized and stored in cells, fluids and skeletal materials secreted by the cells, waste products of metabolism, etc. The same substances also compose the materials taken in by organisms as *foods*, most of which are products of other organisms.

---

[1] The principles of chemical symbolism and terminology are explained briefly in an appendix at the end of this book.

Elementary constituents.—The twelve elements listed below are found in almost all kinds of cells that have been analyzed, and in roughly the same proportions. The figures given are averages of several kinds of plant and animal tissues containing relatively little intercellular material, and represent approximate percentages (by weight) of the tissues in their natural condition.

	Per Cent
Oxygen (O)	76
Hydrogen (H)	10
Carbon (C)	10.5
Nitrogen (N)	2.5
Sulphur (S)	.2
Phosphorus (P)	.3
Potassium (K)	.3
Iron (Fe)	.01
Magnesium (Mg)	.02
Calcium (Ca)	(.02)
Sodium (Na)	(.05)
Chlorine (Cl)	(.10)

Of these elements the first nine are present, and essential to life, in every organism so far as known. Calcium is not essential in some of the lower organisms; sodium and chlorine are not essential in most plants, but they are in animals (at least in the higher ones). These three elements are usually more abundant in the body fluids (*e.g.*, blood) than in the cells themselves.

The same elements are very generally present in intercellular materials and food substances, though in much more variable proportions. Several other elements are constituents of substances essential to life in some but not in most organisms; *e.g.*, fluorine (*F*), bromine (*Br*), iodine (*I*), boron (*B*), silicon (*Si*), manganese (*Mn*), copper (*Cu*), zinc (*Zn*), aluminum (*Al*). All these constituents of protoplasm and its products are also among the most common elements in non-living nature, being found everywhere as constituents of mineral compounds in rocks, soils, and waters. There is no element peculiar to living things, though a few of them—

especially carbon and nitrogen—are relatively more abundant in living than in non-living nature.

Compounds.—None of these elements, except oxygen, usually occur *free* in organisms, or in their foods or waste products, but in the form of chemical *compounds* of various kinds. These compounds are classified into two groups: *inorganic* ("mineral") compounds and *organic* compounds. The former are found in non-living, as well as in living, nature; the latter occur naturally only in organisms and their products.

Inorganic compounds make up the great bulk of non-living nature: the rocks and the soils which are products of their disintegration, water and the various salts which are dissolved in all natural waters, etc. These compounds are, generally speaking, relatively simple (*i.e.*, have small molecules) as compared with organic compounds. They may contain almost any of the chemical elements.

The inorganic components of protoplasm and its products are *water* and certain *salts* and *gases*. All these substances are abundant in non-living nature and are in no way peculiar to organisms, though they play absolutely essential rôles in life processes.

Water is the most abundant single component of protoplasm, which contains about 70–90% (by weight) of this one compound. The proportion varies considerably in different kinds of cells: in general, the younger, more rapidly growing, and more active cells contain the larger proportions of water. This water is by no means an accidental or inert component, but plays an absolutely essential rôle in all the phenomena of life.

The water molecule is made up of one oxygen and two hydrogen atoms (Fig. 3); this molecule is highly *polar*, because the hydrogen atoms are positively charged and the oxygen atom negatively charged (p. 9). Water *dissolves* a greater variety of substances than any other liquid: it is the best solvent for most inorganic compounds and also for many organic substances (carbohydrates, proteins, etc.); this property is due to its highly polar character, which favors the solution of all polar or partly polar substances. For the same reason water promotes, more than any other solvent, the *dissociation* of electrolytes dissolved in it into their constituent ions (p. 10). Water itself dissociates electrolytically, to a slight extent (about one molecule in 555,000,000), into *hydrogen ions* (H^+) and *hydroxyl ions* (OH^-); these two kinds of ions, though present in such relatively small proportions, are very active chemically and electrically. Water promotes, to an unequalled extent, chemical reactions among substances dissolved in it; this is due partly to its great power to ionize these substances, partly to the great chemical activity of its own ions (H^+ and OH^-). The constituent elements of water (oxygen and hydrogen) are also abundant constituents of all the numerous organic compounds in the organism, and water takes direct part, as reactant or resultant, in most or all of the chemical reactions which these compounds undergo in the cell, which constitute metabolism. Some other characteristic properties of water which are of great importance in life processes are its high *cohesion* and *surface tension* (p. 64), its great *fluidity* (low viscosity), and its large *heat capacity* (ability to absorb a large quantity of heat with relatively little change of temperature). In short, water has a unique combination of properties which makes the phenomena of life possible only in a system composed mostly of this substance.

Not only is water the most abundant component of protoplasm itself, but also all living cells are surrounded by water. The unicellular and simplest multicellular organisms all live in water or dilute aqueous solutions; in higher plants and animals the living cells are surrounded by aqueous *body fluids* (sap, blood, or lymph) and the body is usually covered externally by some impervious non-living material (secreted by the cells or composed of dead cells) which prevents excessive evaporation of water from it.

Salts.—The inorganic salts generally found in organisms are those which are also most common in the sea and, in smaller proportions, in fresh waters. These salts are all strong electrolytes and therefore, in dilute aqueous solutions, as they occur in the organism, are largely (or perhaps entirely) dissociated into their constituent ions. The inorganic ions (aside from H^+ and OH^-) most generally present in the cells, body fluids, foods, and waste products of organisms are the following:

Cations	
K^+	potassium
Na^+	sodium
NH_4^+	ammonium
Ca^{++}	calcium
Mg^{++}	magnesium
Fe^{++}	iron
Fe^{+++}	

Anions	
Cl^-	chloride
SO_4^{--}	sulphate
NO_3^-	nitrate
NO_2^-	nitrite
HCO_3^-	carbonate
CO_3^{--}	
$H_2PO_4^-$	phosphate
HPO_4^{--}	
PO_4^{---}	

Of these, nitrate and nitrite are found chiefly in plants, chloride and sodium chiefly in animals, calcium in most organisms, and the others in probably all organisms. These ions, or the salts which they compose, make up roughly 1% (by weight) of protoplasm, and about the same proportion of most body fluids.

These inorganic salts play various rôles in life processes. Some of them—especially those containing carbon, nitrogen, sulphur, phosphorus, and iron—furnish the "raw materials" for the synthesis (especially in plants) of organic compounds. The decomposition of these organic compounds in the destructive (energy liberating) metabolism of the cell produces the same salts again as waste products. Some of the inorganic ions—especially those of the metals—are essential components of protoplasm *as ions*, playing a large part in determining its structure and activities by virtue both of their chemical properties and of their electric charges. Some of the skeletal materials of organisms (*e.g.*, bone, shells) are composed chiefly of inorganic salts (calcium phosphate, calcium carbonate, etc.).

Gases.—*Free oxygen* (O_2), *carbon dioxide* (CO_2), and *ammonia* (NH_3) are present, in varying amounts, in all cells. Free oxygen is an essential food substance of almost all organisms, and is also produced as a waste substance by green plant cells. Carbon dioxide and ammonia are waste products of metabolism of all cells, and also serve as materials for the synthesis of organic compounds in plants.

Ammonia and carbon dioxide react with water, producing ammonium and carbonate ions, respectively:

$$NH_3 + H_2O \rightleftharpoons NH_4OH \rightleftharpoons NH_4^+ + OH^-$$
$$CO_2 + H_2O \rightleftharpoons H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$$

The intermediate products, *ammonium hydroxide* and *carbonic acid*, are supposedly unstable substances which can only exist in aqueous solution.

The maintenance of neutrality.—*Hydrogen* and *hydroxyl ions* are always present in any aqueous solution, since they are produced by the dissociation of water itself:

$$H_2O \rightleftharpoons H^+ + OH^-$$

There are also many other substances (*acids* and *bases*) in the cell which produce hydrogen or hydroxyl ions; *e.g.*, carbon dioxide and ammonia, as shown above, and also many organic compounds. A solution containing more hydrogen than hydroxyl ions is *acidic;* one containing an excess of hydroxyl ions is *basic* (or *alkaline*); a solution containing equal numbers of these two kinds of ions is *neutral.* In pure water or any neutral solution there are relatively few free hydrogen and hydroxyl ions—only one of each to about 555,000,000 water molecules—all the rest recombining to form water molecules. Despite their very small concentrations these ions, because of their great chemical activity, play extremely important parts in life processes. Protoplasm is always very nearly exactly neutral. Any considerable deviation from neutrality, in either direction, is quickly fatal. Although acid and basic substances (especially acids) are being continually produced by metabolic processes in the cells, and also taken in as foods, the neutrality of the protoplasm is maintained without appreciable deviation. This is due to the presence in the cells and the body fluids of substances which have the chemical property of combining with either hydrogen or hydroxyl ions according to which is present in excess. Such substances are called *buffers.* The most important inorganic buffer substances in organisms are the *carbonates* and *phosphates.* When an acid, producing hydrogen ions, is added to neutral solutions of these substances, reactions such as the following occur instantaneously:

$$H^+ + HCO_3^- \rightarrow H_2CO_3$$
$$H^+ + HPO_4^{--} \rightarrow H_2PO_4^-$$

Thus practically all the free hydrogen ions are immediately removed from the solution, which therefore remains neutral or very nearly so. When a base, producing hydroxyl ions, is added to such a solution, the opposite reactions occur:

$$H_2CO_3 + OH^- \rightarrow HCO_3^- + H_2O$$
$$H_2PO_4^- + OH^- \rightarrow HPO_4^{--} + H_2O$$

In this way, solutions containing these substances can absorb large quantities of acids or bases with very little change from neutrality. Many of the organic components (especially proteins) of cells and body fluids are also very efficient buffers, so that the organism is well protected against changes from neutrality under any ordinary circumstances.

Organic compounds are defined as "compounds of carbon and hydrogen, in which some (or all) of the hydrogen may be replaced by other elements or radicals." These compounds are found in nature only in organisms and in the products and remains of organisms; but many of these natural organic compounds, and many others never found in nature, have been synthesized artificially in the chemical laboratory. Organic compounds are, in general, more complex (*i.e.*, have larger molecules) than inorganic compounds; while the molecules of most inorganic compounds consist of from two to a dozen atoms, many organic compounds contain hundreds or even thousands of atoms in a molecule. The primary cause of this greater complexity lies in the peculiar chemical properties of the element carbon. Carbon atoms have the capacity to combine chemically with each other, forming long chains or rings; a single organic molecule may contain hundreds of carbon atoms united in this way. The structure of the carbon atom (having 4 valence electrons) enables it to combine with four other atoms simultaneously; thus each carbon atom in a chain may be attached to one, two, or three atoms or radicals besides its neighboring carbon atoms. Being intermediate in structure between the electro-positive atoms (1–3 valence electrons) and the electro-negative atoms (5–7 valence electrons), carbon can combine with both metallic and non-metallic elements; thus almost any element or radical can be substituted for one or more of the hydrogen atoms in an organic molecule. These properties of carbon make possible the great variety, as well as the great complexity, of its compounds. The number of organic compounds, natural and artificial, which have been actually separated and chemically identified, is in the hundreds of thousands; but the number occurring in living organisms is undoubtedly very much greater than this.

Besides *carbon* and *hydrogen*, practically all the organic compounds found in organisms contain more or less *oxygen;* many of them contain *nitrogen*, and some also *sulphur* or *phosphorus* or both. A few contain other elements (*e.g.*, iron, magnesium) as integral parts of the organic molecule; there are also many organic salts which consist of an organic ion associated with inorganic ions of the various kinds listed above (p. 42).

The molecule of practically every organic compound found in organisms is made up of one or more *hydrocarbon radicals* (CH, CH_2, CH_3) and one or more other kinds of atoms or radicals attached to some of the carbon atoms. The other atoms and radicals most generally found in biologically important organic compounds are O, OH, NH, NH_2, SH, PO_4. The hydrocarbon radicals are nonpolar, but all these others are more or less polar. The organic compounds are more or less polar, depending on the relative proportions of these polar groups and the nonpolar hydrocarbon groups which they contain. Thus, the sugars, which contain many O and OH groups, are highly polar compounds, very soluble in water, while the fats, which consist principally of CH_2 groups, are highly nonpolar, very insoluble in water. Within the same molecule, also, one part may be polar, other parts nonpolar, depending on the arrangement of these different kinds of radicals within the molecule. These peculiarities of organic molecules play a very important rôle in the physical structure of protoplasm, because of the very different solubilities of polar and nonpolar groups (p. 11). They are also important factors in the chemical reactions of metabolism, since polar groups are, in general, more active chemically than nonpolar groups; thus one part of a complex organic molecule may undergo various chemical changes while other parts remain unchanged.

The living cell contains an almost infinite variety of different kinds of organic compounds, continually changing and interacting with each other. But certain kinds, because of their greater chemical stability, accumulate in larger proportions, and form the bulk of the organic components of protoplasm, intercellular materials, and food substances. It is customary to divide these compounds into three general classes, distinguished by chemical and physical differences: the *carbohydrates*, the *lipins*, and the *proteins*. Practically all the organic compounds found in organisms and their products may be regarded as belonging to these three classes, or as stages in the synthesis and decomposition of these.

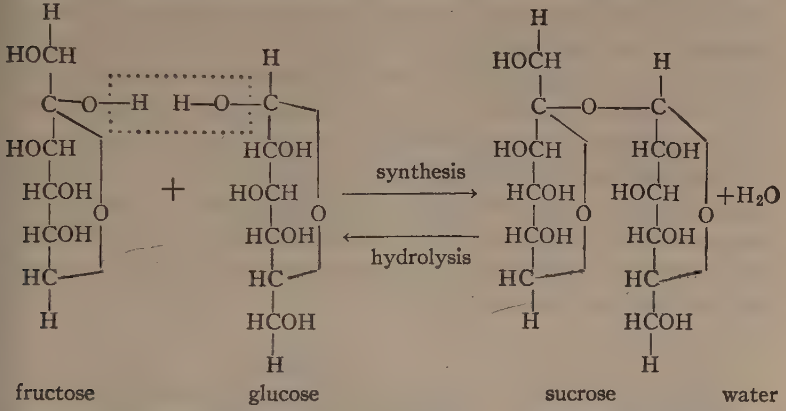
Carbohydrates (sugars, starch, etc.) are compounds of *carbon*, *hydrogen*, and *oxygen*, the last two usually in the same proportion as in water (2 : 1). The carbohydrates found most abundantly in organisms contain chains of six carbon atoms, each molecule consisting of one such chain or of two or more of them united by oxygen atoms. Some of the most important carbohydrates are:

$$\left.\begin{array}{l}\textit{monosaccharoses}, C_6H_{12}O_6\text{: glucose, fructose, galactose, etc.}\\ \textit{disaccharoses}, C_{12}H_{22}O_{11}\text{: sucrose, maltose, lactose, etc.}\end{array}\right\}\text{sugars}$$

polysaccharoses, $(C_6H_{10}O_5)_x$: starch, glycogen, cellulose, etc.

It will be noted that several of these compounds have the same formula, *e.g.*, $C_6H_{12}O_6$; that is, their molecules contain the same numbers of each kind of atoms: the differences among such compounds are due to the different arrangements of the atoms within their molecules, as illustrated by the structural formulas of glucose and fructose shown below. The molecular formulas of the polysaccharoses are large, not exactly known, multiples of $C_6H_{10}O_5$; in starch this multiple is about 200, in cellulose probably much larger. The sugars (mono- and disaccharoses), with relatively small molecules, are very soluble in water. The polysaccharoses, with much larger molecules, are less soluble; cellulose is quite insoluble.

Each molecule of a disaccharose is made up by combination of two monosaccharose molecules (of the same or different kinds) with the elimination of one molecule of water. The disaccharose may be decomposed into its constituent monosaccharoses by *hydrolysis; i.e.*, by chemical combination with water which splits the disaccharose molecule into two monosaccharose molecules. These reactions may be illustrated by the synthesis and hydrolysis of *sucrose* (common sugar):



Similarly, *lactose* is made up of *glucose* and *galactose; maltose*, of *two* molecules of *glucose.* Starch, glycogen, and cellulose are each made up of many molecules of glucose, minus the corresponding number of water molecules, but the molecular structures of these complex polysaccharoses are not yet completely known. The hydrolysis of these substances is a series of successive reactions, forming a series of simpler polysaccharoses called *dextrins*, then maltose, and finally glucose.

These reactions—hydrolysis and dehydrolytic synthesis—play important parts in the metabolism of carbohydrates in organisms. In living cells, the di- and polysaccharoses are thus synthesized from monosaccharoses. In the digestive tract of animals and also within the cells of all organisms, di- and polysaccharoses are hydrolyzed into their constituent monosaccharoses. The conditions under which these reactions occur will be considered later (Chapter VI).

Carbohydrates are of great importance in organisms as fuel, as stored foods, and as structural materials. *Glucose* is the primary fuel substance of almost all organisms; its oxidation in the cell furnishes the energy for all the activities of the organism. Other monosaccharoses may serve in the same way; but they are apparently first converted into glucose, at least in many organisms, before oxidation. *Starch* is the principal stored food substance in most plants; it is stored in the cells in the form of granules, whose size and shape differ in different kinds of plants (Fig. 15). Other polysaccharoses and some disaccharoses, especially *sucrose*, also serve as stored food materials in plants. *Glycogen* ("animal starch") plays a similar rôle in animals. *Lactose* ("milk sugar") is found in the milk of all mammals, and is therefore an important food substance of the young of these animals. *Maltose* ("malt sugar") occurs chiefly as an intermediate stage in the hydrolysis of starch. *Cellulose* forms the cell walls surrounding all plant cells; it is the chief component of wood. Monosaccharoses and closely related compounds also occur as constituent radicals of more complex organic substances.

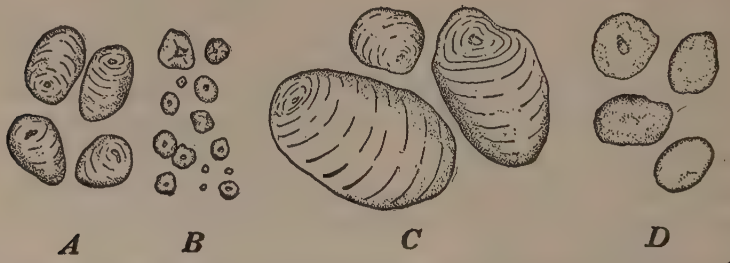
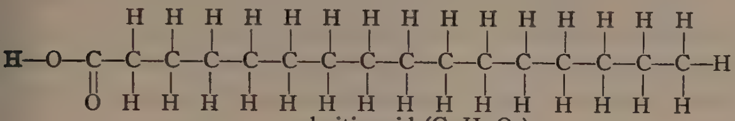


Fig. 15.—Starch grains from different plants, all drawn to the same scale: *A*, arrowroot; *B*, corn; *C*, potato; *D*, wheat.

Lipins (fatty substances) are predominantly nonpolar compounds, and therefore insoluble in water but soluble in various organic liquids, *e.g.*, ether, chloroform, gasoline, hot alcohol, etc. All lipins contain *carbon*, *hydrogen*, and *oxygen*, but the last in much smaller proportions than in carbohydrates. Some of them (phospholipins) also contain *nitrogen* and *phosphorus*. Some lipins are liquid ("oils"), others solid ("fats," "waxes") at ordinary temperatures, but all are characteristically "greasy" substances. There is a great variety of compounds, of diverse chemical constitution, found in organisms, having these general characteristics, and included in the term "lipins." Those of most general biological importance are:

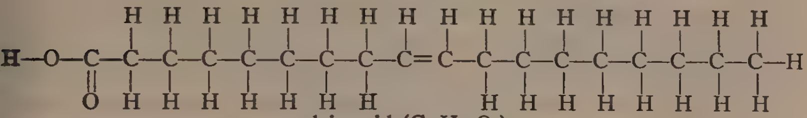
true *fats:* lard, butter, olive oil, etc.
phospholipins: lecithin, etc.
sterols: cholesterol, etc.

The true *fats* are *esters* of *glycerol* and *fatty acids*. A large number of different fatty acids are found in organisms; they are all straight chains of an even number of carbon atoms, with a single acid group (containing *ionizable* hydrogen) at one end; the most common ones have 16 or 18 carbon atoms. Their molecular structures are exemplified by the following (the heavy H represents *ionizable* hydrogen):



$$\mathbf{H}{-}O{-}\underset{\underset{O}{\|}}{C}{-}\underset{H}{\overset{H}{C}}{-}\underset{H}{\overset{H}{C}}{-}\underset{H}{\overset{H}{C}}{-}\underset{H}{\overset{H}{C}}{-}\underset{H}{\overset{H}{C}}{-}\underset{H}{\overset{H}{C}}{-}\underset{H}{\overset{H}{C}}{-}\underset{H}{\overset{H}{C}}{-}\underset{H}{\overset{H}{C}}{-}\underset{H}{\overset{H}{C}}{-}\underset{H}{\overset{H}{C}}{-}\underset{H}{\overset{H}{C}}{-}\underset{H}{\overset{H}{C}}{-}\underset{H}{\overset{H}{C}}{-}\underset{H}{\overset{H}{C}}{-}H$$

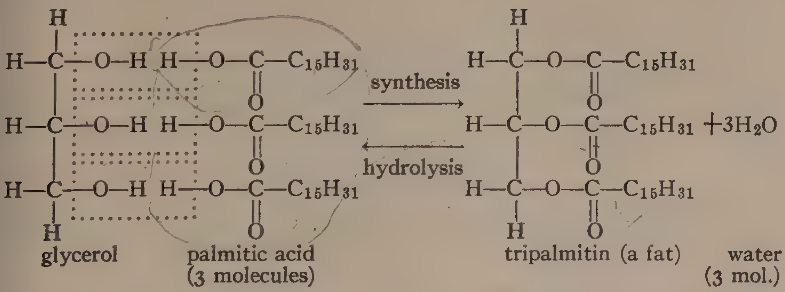
palmitic acid ($C_{16}H_{32}O_2$)



$$\mathbf{H}{-}O{-}\underset{\underset{O}{\|}}{C}{-}\underset{H}{\overset{H}{C}}{-}\underset{H}{\overset{H}{C}}{-}\underset{H}{\overset{H}{C}}{-}\underset{H}{\overset{H}{C}}{-}\underset{H}{\overset{H}{C}}{-}\underset{H}{\overset{H}{C}}{-}\underset{H}{\overset{H}{C}}{-}\overset{H}{C}{=}\overset{H}{C}{-}\underset{H}{\overset{H}{C}}{-}\underset{H}{\overset{H}{C}}{-}\underset{H}{\overset{H}{C}}{-}\underset{H}{\overset{H}{C}}{-}\underset{H}{\overset{H}{C}}{-}\underset{H}{\overset{H}{C}}{-}\underset{H}{\overset{H}{C}}{-}\underset{H}{\overset{H}{C}}{-}H$$

oleic acid ($C_{18}H_{34}O_2$)

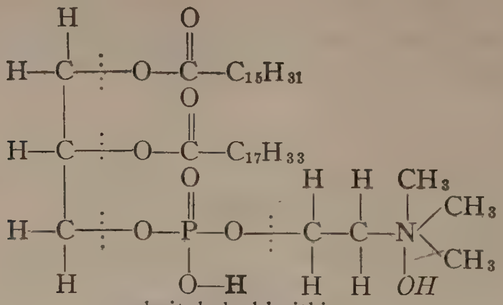
The other fatty acids differ from these only in the number of carbon and hydrogen atoms. Those with the maximum possible number of hydrogen atoms, like palmitic acid, are called *saturated;* those with a smaller proportion of hydrogen to carbon, like oleic acid, are called *unsaturated.* Each molecule of a fat is made up by combination of one glycerol molecule with three fatty acid molecules (of the same or different kinds), with the elimination of three molecules of water; *e.g.:*



The fats may be decomposed into glycerol and fatty acids by hydrolysis, as indicated above. Fats are also decomposed by alkalies (sodium or potassium hydroxide) into glycerol and the sodium or potassium salts of the fatty acids; these salts are *soaps,* and this reaction is called *saponification.* The soaps, unlike the fats and fatty acids, are quite soluble in water. Fats are synthesized from glycerol and fatty acids, as shown above, in living cells; they are hydrolyzed (and, to some extent, saponified) in the digestive tract of animals as well as within cells.

Different fats melt at different temperatures, depending on the kinds and proportions of the different fatty acids they contain. Most fats are liquid at the normal body temperatures of the organisms in which they occur. Those liquid at ordinary room temperature (about 20° C) are commonly called "oils"; *e.g.*, olive oil, cod liver oil, etc. The fats of warm-blooded animals, whose body temperatures are about 37° C, are solid or semi-solid at room temperature; *e.g.*, lard, tallow, etc.

The *phospholipins* are more complex than the true fats, containing, besides *glycerol* and *fatty acids*, *phosphoric acid* and *organic bases*. They can be decomposed into these substances by hydrolysis or saponification. The most common phospholipins are the *lecithins*, in which the basic radical is *choline;* different lecithins contain different fatty acids, but always at least one unsaturated one. The molecular structure of lecithin is:



palmityl-oleyl-lecithin

(**H**=ionizable hydrogen; *OH*=ionizable hydroxyl; the dotted lines indicate the points at which the molecule is split by hydrolysis.)

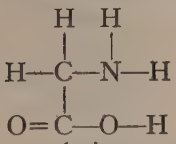
The phospholipins are fat-like substances, semi-solid at ordinary temperatures. They have relatively more polar radicals than the true fats (as shown in the structural formulas above), and therefore have a greater affinity for water. In contact with water they swell up to many times their own volume by absorbing water, although they do not actually dissolve in the water to any great extent. Phospholipins are the most abundant lipins in most cells.

The *sterols* are very complex compounds, containing many carbon and hydrogen atoms and one OH radical; they can not be decomposed by hydrolysis or saponification. They are wax-like substances, very insoluble in water. The best known example is *cholesterol* ($C_{27}H_{45}OH$). This or closely related compounds are present in all cells, partly in combination with fatty acids as esters. These sterol esters have the same physical characteristics as the sterols themselves; but they can be decomposed by hydrolysis or saponification like other esters.

Phospholipins and sterols are essential components of all protoplasm; their importance in its structure will be discussed in the next chapter. True fats are the principal stored food substances in animals and in some plants. Glycerol and fatty acids can be oxidized in the cell, yielding energy. Fats and carbohydrates are interconvertible in the living organism.

Proteins are the most complex of all chemical compounds, containing thousands of atoms to the molecule. All natural proteins contain *carbon*, *hydrogen*, *oxygen*, *nitrogen*, and *sulphur;* many also contain *phosphorus*. A few of them contain other elements (*e.g.*, iron) as integral parts of the molecule. Proteins, as they actually occur in the living cell, are mostly in the form of ions, associated with various inorganic ions (especially potassium); but these inorganic ions are customarily not regarded as part of the protein.

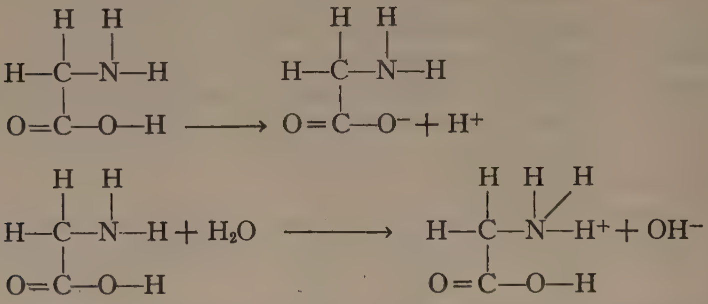
All proteins are made up, either entirely or largely, of simpler organic substances called *amino-acids*, chemically combined to form the protein molecules. The molecular structure of the simplest amino-acid is:



$$\begin{array}{ccccccc} & & \mathrm{H} & & \mathrm{H} & & \\ & & | & & | & & \\ \mathrm{H} & - & \mathrm{C} & - & \mathrm{N} & - & \mathrm{H} \\ & & | & & & & \\ \mathrm{O} & = & \mathrm{C} & - & \mathrm{O} & - & \mathrm{H} \end{array}$$

glycine

Other amino-acids differ from this only in having one of the hydrogens of the CH_2 group replaced by organic radicals of various degrees of complexity. Every amino-acid contains at least one *carboxyl* radical (COOH) and one *amino* radical (NH_2). The carboxyl radical always acts as an acid (dissociates hydrogen ion), while the amino radical acts, like ammonia (p. 42), as a base. Thus the amino-acids can dissociate, in water, in these two ways:

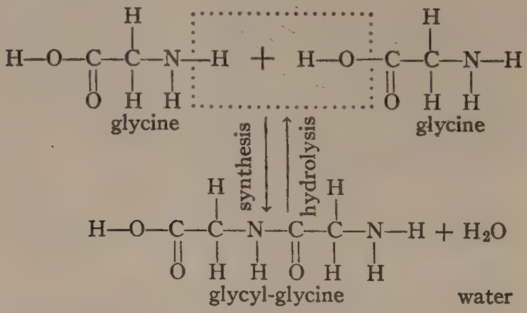


$$\mathrm{H{-}\underset{\displaystyle O{=}C{-}O{-}H}{\overset{H}{C}}{-}\overset{H}{N}{-}H \longrightarrow H{-}\underset{\displaystyle O{=}C{-}O^{-}}{\overset{H}{C}}{-}\overset{H}{N}{-}H + H^{+}}$$

$$\mathrm{H{-}\underset{\displaystyle O{=}C{-}O{-}H}{\overset{H}{C}}{-}\overset{H}{N}{-}H + H_2O \longrightarrow H{-}\underset{\displaystyle O{=}C{-}O{-}H}{\overset{H}{C}}{-}\overset{H\;H}{N}{-}H^{+} + OH^{-}}$$

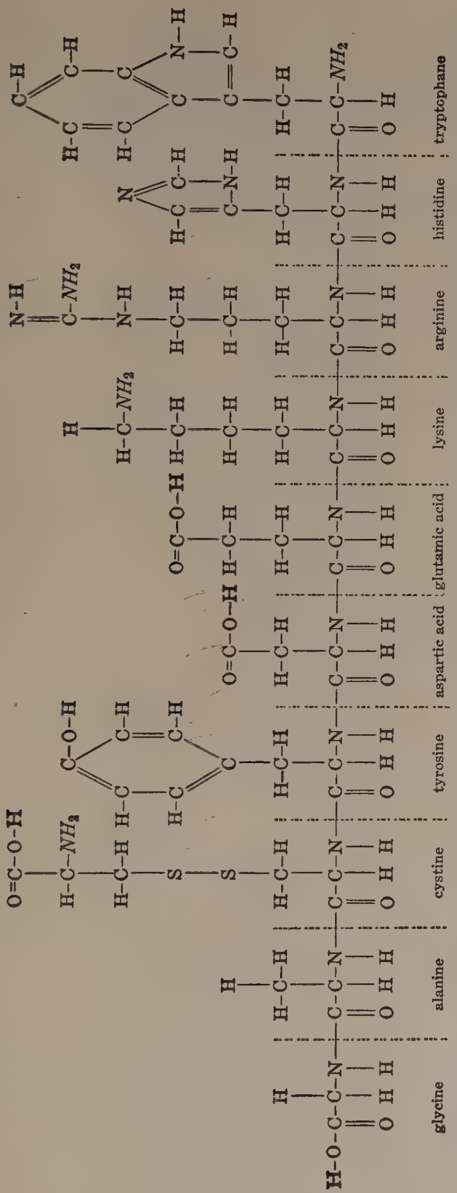
These compounds act, therefore, both as acids and as bases. In basic solutions they dissociate chiefly as acids; in acidic solutions chiefly as bases; in neutral solutions some amino-acids are more acidic, others more basic. The proteins have these same properties. Most natural proteins are somewhat more acidic than basic; in neutral solutions, such as protoplasm, they exist therefore chiefly as *anions*.

The amino-acids are combined in the protein molecule, through the amino radical of one and the carboxyl radical of another, in this way:



$$\mathrm{H{-}O{-}\underset{\displaystyle \overset{\|}{O}}{C}{-}\underset{H}{\overset{H}{C}}{-}\underset{H}{N}{-}H + H{-}O{-}\underset{\displaystyle \overset{\|}{O}}{C}{-}\underset{H}{\overset{H}{C}}{-}\underset{H}{N}{-}H \rightleftarrows H{-}O{-}\underset{\displaystyle \overset{\|}{O}}{C}{-}\underset{H}{\overset{H}{C}}{-}\underset{H}{N}{-}\underset{\displaystyle \overset{\|}{O}}{C}{-}\underset{H}{\overset{H}{C}}{-}\underset{H}{N}{-}H + H_2O}$$

This synthesis, it will be noted, still leaves a free carboxyl radical at one end and a free amino radical at the other, so that additional amino-acid molecules can be added on; in this way long chains of amino-acids are built up. This method of combination between amino-acids is called the *peptide linkage*, and the compounds thus formed are called


glycine
alanine
cystine
tyrosine
aspartic acid
glutamic acid
lysine
arginine
histidine
tryptophane

A hypothetical polypeptide consisting of ten different amino-acids (**H** = ionizable hydrogen; NH_2 = free amino (basic) group; the dotted lines indicate the points at which the molecule is split by hydrolysis).

polypeptides. The proteins are compounds of this type; they are synthesized in living cells, and they are decomposed into their constituent amino-acids by hydrolysis of the peptide linkages, as indicated above. A polypeptide containing ten different amino-acids is shown on p. 53, illustrating the type of structure of protein molecules; it will be noted that, because some of the individual amino-acids have two carboxyl or two amino radicals, there are always a number of free acid and basic groups in the protein molecule. Proteins have been synthesized artificially, containing as many as 18 amino-acid molecules combined by peptide linkages. The natural proteins contain some hundreds of amino-acid molecules in each protein molecule. Only about 20 different amino-acids are found in natural proteins, but differences in the proportions and arrangement of these in the protein molecule give a practically infinite number of chemically distinct proteins. Very few, if any, of these natural proteins have been separated as chemically pure substances; but certain biological tests show that there are differences among the proteins of closely related species of organisms and even of individuals of the same species, as well as among the proteins of different tissues in the individual.

The proteins are divided into several classes on the basis of their chemical and physical characteristics. The two main classes are *simple proteins*, composed entirely of amino-acids, and *conjugated proteins*, which contain other radicals besides the amino-acids. The simple proteins are further subdivided chiefly on the basis of their solubilities: they include *albumins* and *globulins*, soluble proteins found in cells, body fluids and other liquid secretions (milk, egg-white, etc.); *scleroproteins*, insoluble proteins found in skeletal and other intercellular materials; and several other groups. The conjugated proteins are classified according to the nature of their radicals other than amino-acids: *phosphoproteins* contain phosphate radicals; *glycoproteins* contain carbohydrate radicals; *hemoglobins* contain *hematin* ($C_{34}H_{34}N_4O_5Fe$), a complex organic acid; *nucleoproteins* contain *nucleic acid* ($C_{38}H_{49}O_{29}N_{15}P_4$); *lipoproteins* contain lipins (fatty acids, phospholipins, etc.).

The hydrolysis of proteins is a series of successive reactions, forming a series of simpler polypeptides called *pro-*

teoses and *peptones*, then very simple peptides (tri- and dipeptides), and finally amino-acids.

Proteins are the most characteristic and, next to water, the most abundant components of protoplasm. Many different proteins are present in every cell. These compounds play many important rôles in the phenomena of life. The large size of their molecules, and other physical properties, are essential to the structure of protoplasm. The great variety and complexity of their chemical constitution (containing nonpolar and polar groups, acid and basic radicals, etc.) enable them to react in many ways with a great variety of other substances; this is the basis of the enormously complex system of chemical interactions which constitutes metabolism. By virtue of their capacity to combine with both acids and bases, the proteins are the most efficient buffer substances (p. 43) in protoplasm and body fluids. Proteins and amino-acids can be converted, in the organism, into carbohydrates and related compounds, thus indirectly serving as fuel for the cells. In some kinds of cells (especially in seeds and eggs) proteins are deposited as stored food substances. *Hemoglobin* in the blood of many animals, and closely related proteins in all cells, play essential rôles in respiration and oxidation. *Nucleoproteins* compose chromatin, the characteristic material of the nucleus; these substances are present in all living cells, even those (bacteria) which have no structurally distinct nucleus, and seem to be essential to the fundamental life processes of assimilation, growth, and reproduction. *Scleroproteins* are the principal organic components of the skeletal structures and other hard parts (outer skin, hair, nails, horns, etc.) of animals. Many other proteins and their derivatives (amino-acids, etc.) perform specific functions, chemically or physically, in various organisms; some of these will be mentioned in subsequent chapters.

Other organic compounds.—A great variety of other, usually simpler, organic compounds is found in organisms and their products. Many of these figure as constituent radicals or decomposition products of carbohydrates, lipins, or proteins. Most of these simpler organic compounds are soluble in water, and are grouped under the general term *extractives*. Many of these substances, though found in only very minute amounts in the cells, may nevertheless be of great importance in the life processes of the organism, as they are necessary intermediate stages in the chemical transformations of metabolism.

The composition of protoplasm.—All living cells contain water, inorganic salts, proteins, and lipins, together with small amounts, at least, of many other substances. These four classes of substances may be regarded as the essential components of protoplasm itself, while the other substances figure chiefly as food and waste materials; this distinction, however, is largely arbitrary. The relative amounts of these different kinds of substances vary considerably in different cells: animal cells generally contain more lipins, plant cells more carbohydrates; younger cells generally contain more water, older cells more solids, etc. The following may be taken as a rough average of the chemical composition of protoplasm from many kinds of cells and organisms, the proportions being expressed as percentages by weight:

	Per Cent
Water	80
Inorganic salts	1
Proteins	15
Lipins (chiefly phospholipins and sterols)	3
Other substances (carbohydrates, extractives, etc.)	1

In the living condition, these substances are chemically combined, to a large extent, into still more complex compounds. Proteins are combined with inorganic ions, with fatty acids, with phospholipins, etc.; sterols are combined with fatty acids and perhaps with phospholipins; carbohydrates are combined with phosphates; part of the water is chemically combined with the substances dissolved in it; etc. Among such complex substances it is practically, and even theoretically, impossible to distinguish sharply between chemical combinations and physical combinations.

Even from the purely chemical standpoint, protoplasm is thus incomparably more complex than any other system, natural or artificial. No chemical compounds as complex as the natural proteins are found elsewhere in nature, or have yet been made artificially in the laboratory. And the still more complex combinations in which these occur in the living cell are as yet not even fully known, as our methods of extracting them from the tissues tend to break up these unstable complexes. While there is still much to be learned about the chemical composition of protoplasm, we do know enough about it to feel confident that the variety and complexity of its components are undoubtedly sufficiently great to account for the enormous variety and complexity of the structures and activities of living things.

CHAPTER IV

PHYSICO-CHEMICAL STRUCTURE OF PROTOPLASM

The largest protein molecules, so far as known, are probably about 6×10^{-7} cm. (6 mμ) in diameter; most other molecules are much smaller than this. The smallest particles visible with the microscope are a little over 10^{-5} cm. (100 mμ) in diameter; that is, about 20 times the diameter of the largest chemical molecules. The smallest microscopically visible particle therefore contains at least several thousand molecules (volume is proportional to the *cube* of diameter; $20^3 = 8000$). Below the limit of microscopic vision, therefore, there is still plenty of room for complex structural relations over and above the internal structures of the individual molecules. These structural relations are partly chemical, partly physical (*i.e.*, non-chemical), in nature; it is really quite impossible to distinguish sharply between chemical and physical relations in a very complex system such as protoplasm. We therefore call the supra-molecular but submicroscopic structure of protoplasm its *physico-chemical structure* as distinguished, though not very sharply, from its purely chemical structure (*i.e.*, the internal structures of its component molecules, discussed in Chapter III) on the one hand, and its microscopically visible structure (discussed in Chapter II) on the other hand. In this field of physico-chemical structure we must seek the explanations of many of the properties and activities of living matter.

Physical state of protoplasm.—Matter exists in three physical states, *solid*, *liquid*, and *gas*, which differ in the relative distances and consequent freedom of movement of the molecules. In a gas the molecules are very far apart and there is no cohesion (inter-molecular attraction) among them; a gas therefore has no definite volume or shape. In a liquid the molecules are much closer together, and their cohesion holds the liquid together in a definite volume; the individual molecules, however, are still free to move about at random within this volume, so that a liquid has internal mobility and changeability of external form. In a solid molecular cohesion is still greater, the movements of the molecules are very restricted, and there is consequently little internal mobility or plasticity of form. The distinction between liquid and solid, however, is not always a sharp one, especially in complex mixtures. The *viscosity* of liquid systems varies from very fluid (like pure water) through thick liquids (like molasses) and soft jellies to the consistency of solids.

Protoplasm is essentially a liquid system; indeed, the liquid state is the only one in which its characteristic activities would be possible. The cohesion characteristic of liquids, as distinguished from gases, is essential to the maintenance of form and continuity. On the other hand, the internal mobility which distinguishes fluids from solids is essential to many of the physical activities of protoplasm, *e.g.*, muscular movement. The manifold chemical reactions which constitute metabolism also require the intimate admixture of substances only possible in a fluid system.

The most abundant component of protoplasm, as we have seen, is water. This liquid combines the properties of high cohesion and low viscosity (p. 41). The viscosity of protoplasm, however, is usually much greater than that of pure water, due to the other substances in it. The consistency of protoplasm varies greatly, not only in different cells but also in different parts of a cell and even in the same part at different times. At one extreme, it may be almost as fluid as water; at other times or places, it is an extremely viscous liquid; often it is a firm, apparently solid, *gel;* this type of solid structure, however, really contains a large amount of liquid (p. 71). Some of the factors involved in these differences and changes of viscosity will appear in the following paragraphs.

Dispersions.—In protoplasm there are many kinds of particles, ranging in size from simple inorganic molecules and ions to microscopically visible granules and droplets. Any mixture of this kind, in which one or more substances are distributed through another substance, is called a *dispersion;* the continuous substance (*e.g.*, water) is called the *dispersion medium*, and the other components are called *dispersed particles.* Dispersions are classified according to the nature and size of the dispersed particles and their relations with the dispersion medium. The various types of dispersions, however, all grade into each other without sharp distinctions, so that it is impossible to give very exact definitions of the terms used in describing them.

A dispersion in which the dispersed particles are separate molecules or ions is called a *solution;* one in which each dispersed particle consists of several or many molecules is called a *suspension* if the particles are solid, or an *emulsion* if they are liquid. On the basis of the size of the dispersed particles, dispersions are classified as *crystalloidal* (particles $<10^{-7}$ cm. in diameter), *colloidal* (particles between 10^{-7} and 10^{-5} cm.) and *coarse* (particles$>10^{-5}$ cm.) A dispersion may be a purely physical mixture or there may be more or less chemical combination between the dispersed particles and the dispersion medium; in the latter case the dispersed particles are said to be *solvated* (or, when the dispersion medium is water, *hydrated*).

Size and visibility of particles.—The lower limit of *macroscopic*, or naked eye, visibility is roughly about 10^{-2} cm. (0.1 mm.), though of course this depends largely on the intensity of light, contrast between the particle and the background, etc. The lower limit of *microscopic* visibility is a little over 10^{-5} cm. (0.1μ); this depends somewhat on the quality (color) of light and certain characteristics of the lens system used, but essentially this limit is set by the nature of light itself. A particle smaller than this cannot *reflect* light and therefore cannot form a definite image. Particles smaller than this, however, may *diffract* light, resulting in a cloudy appearance of dispersions containing such particles. Particles which diffract light, though too small to reflect it, may be "seen," in a sense, by means of the *ultramicroscope.* This instrument is similar to the ordinary compound microscope except that the light is thrown on the object from the side instead of from below; dispersed particles, therefore, appear as light spots against a dark background (Fig. 16). With this instrument, under the best conditions of illumination, particles down to about 10^{-7} cm. ($1 m\mu$) in diameter—that is, about one-hundredth of the diameter of the smallest true microscopic particle—appear as points or specks of light, due to diffraction. These *diffraction images* give no indication of the true size, shape, or color of such particles, but do show their number and motions. Such particles are called *ultramicroscopic*. Particles still smaller than this, as most molecules are, do not appear as separate points of light but merely form a diffuse haze in the field of the ultramicroscope; these particles are called *amicroscopic*.

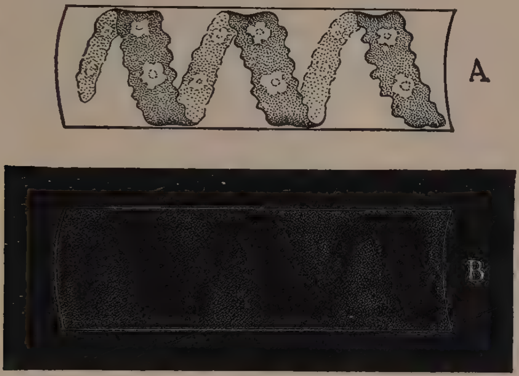
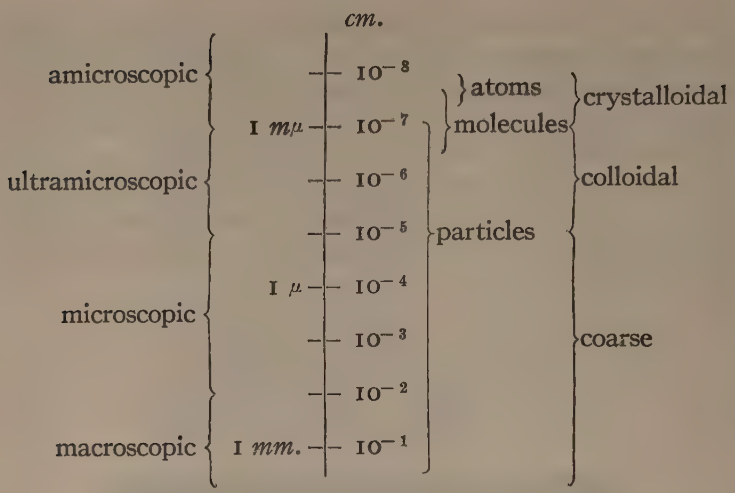


FIG. 16.—A cell of Spirogyra, as seen (*A*) with a high power microscope with ordinary illumination, (*B*) with "dark field" illumination or ultramicroscope. The actual magnification is the same in both cases, but the numerous ultramicroscopic particles which are quite invisible in *A*, appear in *B* as bright specks. Some of the structural details, shown in Fig. 14, are omitted from these drawings. (Adapted, in part, from Gaidukov.)

Particles above 10^{-5} cm. in diameter—microscopic or macroscopic—are called *coarse*. Particles between 10^{-7} and 10^{-5} cm. (1–$100\ m\mu$) in diameter—that is, of ultramicroscopic dimensions—are called *colloidal:* these include the largest organic molecules (those of proteins, starch, etc.) and also particles made up of several or many molecules of any kind. Most molecules (those of inorganic and the simpler organic substances) are between 10^{-8} and 10^{-7} cm. in diameter; these are called *crystalloidal*.

These size relations are summarized in the diagram on the following page.

It must be remembered, of course, that the scale of size in this diagram is a logarithmic scale; that is, each of the equal intervals represents a range ten times as great as the preceding one.


cm.
amicroscopic
ultramicroscopic
microscopic
macroscopic
1 mμ
1 μ
1 mm.
10^{-8}
10^{-7}
10^{-6}
10^{-5}
10^{-4}
10^{-3}
10^{-2}
10^{-1}
atoms
molecules
particles
crystalloidal
colloidal
coarse

Brownian movement.—The colloidal particles seen in the ultramicroscope are always in irregular, rapid movement. The larger suspended particles visible in the ordinary microscope show similar, but slower, movements. This is called *Brownian movement.* It is due to the bombardment of these particles by the water molecules, which, like all molecules of liquids and gases, are in continual random movement; this molecular movement constitutes *heat,* and its intensity is what we measure as *temperature.* At any given temperature, the velocities of different particles are inversely proportional to the square roots of their masses; *e.g.*, a particle 10,000 times as heavy as a water molecule would move only 1/100 as rapidly. Thus the large molecules of proteins and polysaccharoses move much more slowly in a solution than the small molecules of water, inorganic salts, etc.; and the much larger suspended particles of microscopic size move still more slowly.

Solutions are mixtures in which one substance is dispersed in the form of separate molecules or ions throughout another substance; the dispersed substance is called the *solute,* the dispersion medium the *solvent.* Most solutions in water are not, however, purely physical mixtures: there is more or less chemical combination between the solute molecules or ions and water molecules; this combination is called *hydration.* Not all the water in such a solution, of course, is thus combined with the solute; usually only a very small fraction of it: the solution therefore consists of hydrated solute molecules, or ions, physically mixed with uncombined water molecules.

Solutions are divided into two classes, according to the size of the solute molecules. In practice, the distinction is made on the basis of the ability of the dissolved substance to pass through a membrane such as parchment: substances which diffuse through such a membrane are called *crystalloids*, those which do not are called *colloids*. A membrane, such as parchment, which permits the passage of crystalloidal solutes, but not of colloids, is called a *dialyzing* membrane. The upper limit of diameter of crystalloidal molecules is about 10^{-7} cm.; the smallest molecules and ions have diameters somewhat over 10^{-8} cm. Practically all inorganic substances in true solution are crystalloids; and also many of the simpler organic compounds. The substances in crystalloidal solution in protoplasm include inorganic salts, sugars, amino-acids, glycerol, and many other organic compounds of relatively small molecular size (extractives). The proteins, polysaccharoses, and phospholipins, in so far as they are in true solution at all, form colloidal solutions, because their individual molecules are over 10^{-7} cm. in diameter.

The dispersed particles of a solute, whether crystalloidal or colloidal, may be ions or undissociated molecules. Solutes which are chiefly, or entirely, in the form of ions are called *strong electrolytes*. Those which are chiefly in the form of undissociated molecules, with a relatively small proportion of ions, are called *weak electrolytes*. Those which are entirely, or very nearly entirely, in the form of undissociated molecules are called *non-electrolytes*. Most salts, both inorganic and organic, are strong electrolytes. Most organic acids and bases, including amino-acids, proteins, and phospholipins, are weak electrolytes. Other organic compounds, such as sugars, glycerol, and fats, are regarded as non-electrolytes, although some of them are ionized to a very slight extent, less than one molecule in a million being dissociated into ions.

Suspensions and emulsions are dispersions in which the dispersed particles are multi-molecular, *i.e.*, consist each of several or many molecules. In a suspension the dispersed particles are solid, in an emulsion they are liquid. In general, however, there is no sharp distinction between these two kinds of dispersions, and the two terms are often used interchangeably. The size of the dispersed particles may range from colloidal to microscopic or even macroscopic dimensions. The particles may be more or less ionized and more or less hydrated.

Many of the components of protoplasm are in the form of suspended or emulsified particles, ranging in size from colloidal particles of proteins, lipins, and polysaccharoses, to microscopically visible particles such as starch grains, pigment granules, fat droplets, etc. (p. 26).

The physically distinct components—liquid and solid, or two separate liquids—of a suspension or emulsion are called its *phases*. Each phase may be a solution composed of two or more chemical components; the components of a solution are not regarded as separate phases. The stability and other properties of a suspension or emulsion depend largely on conditions at the *surface* of contact between the two phases.

Surface tension.—A liquid differs from a gas in that its molecules are sufficiently close together so that the attractive forces between them become effective; this constitutes the *internal pressure* of liquids. It differs from a solid, on the other hand, in that its molecules are free to move about at random (Brownian movement) within the volume occupied by the liquid. In the interior of the liquid, each molecule is attracted equally in all directions by the neighboring molecules, so that the *resultant* force acting on it is zero. A molecule at the surface of the liquid, however, is attracted inward and sideways by neighboring molecules, but not outward; it is therefore acted on by a resultant force pulling it toward the interior of the liquid (Fig. 17). Consequently there exists at every liquid surface a layer in which the molecules are relatively restricted in their movements, and which therefore has somewhat the properties of a solid. This layer is called the *surface film*. Because of the sidewise pull of the surface molecules on each other, the surface film of a liquid acts like a stretched elastic membrane: it tends to contract as much as possible; if it is weakened at any point, it contracts in all directions away from this point. This force is called *surface tension*. The surface tension of a liquid is, like its internal pressure, due to the attractive forces between its molecules (cohesion), and is, therefore, greatest in those liquids in which this molecular attraction is strongest; namely, in the most highly polar liquids. Water has the highest surface tension of any liquid except mercury.

Surface tension and a surface film exist not only at the surface of a liquid in contact with air, but also at every surface of contact between a liquid and a solid or between two liquids. The greater the surface tension at the interface between two phases, the less is their tendency to mix or dissolve in each other. Anything, therefore, which lowers this interfacial surface tension will favor dispersion of the one substance in the other.

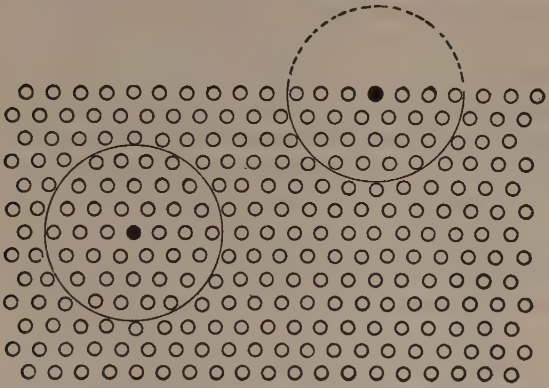


FIG. 17.—Diagram to illustrate the theory of surface tension. The small circles represent the molecules of the liquid. The large circles represent the "spheres of attraction" of the molecules represented by the black circles, *i.e.*, the distances within which the inter-molecular attractive forces are effective. It is readily seen that the forces thus acting on the "interior" molecule are completely balanced, while the surface molecule is subject to a resultant force toward the interior of the liquid.

This surface tension, or tendency of the surface film to contract, can obviously do work (produce movement); it is, therefore, a form of potential energy. Whenever the surface tension is decreased by any means, this *surface energy* must be converted into some other form of energy; *e.g.*, heat, mechanical energy, etc. Many of the activities of cells probably involve such transformations of surface energy.

Because of the enormous extent of surfaces of contact between different phases in such a mixture as protoplasm, surface forces play a very great part in its structure and activities.

Effects of dissolved substances on surface tension.—The internal pressure and the surface tension of a solution may be greater or less than those of the pure solvent, according as the attractive forces between the solute and the solvent molecules are, on the whole, greater or less than those among the solvent molecules themselves. Strongly polar substances, such as inorganic salts, attract water molecules more strongly than the latter attract each other. The internal pressure of solutions of such substances is, therefore, greater than that of pure water. The attraction between the solute and the water molecules tends to pull the former into the interior of the liquid, so that their concentration is smaller in the surface film than in the rest of the solution. For this reason, the effect of such solutes on the surface tension is much less than their effect on the internal pressure; they increase the surface tension, but only very slightly.

On the other hand, substances which are on the whole less strongly polar than water itself attract the water molecules less strongly than the latter attract each other. Solutions of such substances, therefore, have lower internal pressure and lower surface tension than pure water. The greater attraction of the water molecules for each other also tends to "squeeze out" the molecules of such solutes, so that they accumulate in the surface film; their effect in lowering the surface tension is, therefore, much greater than their effect on the internal pressure. Substances such as hydrocarbons, which are entirely nonpolar and therefore have no attraction at all for water, are "squeezed out" entirely; *i.e.*, they are insoluble in water. But polar-nonpolar compounds (having some polar radicals and some nonpolar radicals) attract the water molecules by their polar radicals, while their nonpolar parts tend to be "squeezed out." Such substances—*e.g.*, fatty acids, soaps, proteins, etc.—therefore form a film on the surface of the water, with their polar radicals directed inward and their nonpolar groups outward. The merest trace of such *surface-active* substances lowers the surface tension of water enormously, since almost the whole of the solute may be concentrated in the surface film. In more concentrated solutions, such substances may accumulate at the surface to such an extent as to form a visible solid crust on it.

These surface-active solutes accumulate in this way, not only at the water surface in contact with air, but also at every surface of contact between water and an "oily" (nonpolar) liquid. The nonpolar radicals of the solute tend to dissolve in the oil, their polar radicals in the water (Fig. 18). These two parts of the molecule are held together by their chemical affinity or electrostatic attraction; therefore, the substance must accumulate in the surface between the two liquids. This phenomenon, the concentration of a solute at the interfacial surface between two phases, is called *adsorption.* From the mechanism of this process, as explained above, it is evident that any solute which lowers the surface tension of a solvent will be adsorbed at its surface; and conversely, any adsorbed substance must lower the surface tension at the surface where it is adsorbed. Adsorption, therefore, decreases the surface energy, which is thereby transformed into heat or some other form of kinetic energy.

Emulsifying agents.—If oil (or other nonpolar liquid) be shaken up with water, an emulsion is formed consisting of small oil drops dispersed in the water; but these will quickly come to the top and coalesce to form a separate layer of oil. This happens because the oil drops are "squeezed out" and squeezed together by the greater attraction of the water molecules for each other; that is, by the surface tension of the water at the oil-water phase boundary. If, however, a small amount of soap or protein be dissolved in this water, the oil will remain permanently emulsified. Such substances, which stabilize an emulsion, are called *emulsifying agents.* Any substance which is adsorbed at the interface between two liquid phases acts as an emulsifying agent, by lowering the surface tension at the phase boundary and also by coating the drops of the dispersed liquid with a film which prevents their coalescence.

There are many surface active substances of this kind in protoplasm: proteins, soaps, fatty acids, phospholipins, etc.

These are adsorbed at the interfaces between watery and "oily" (lipin) phases, and thus keep them emulsified.

The form of an emulsion—that is, which liquid is the *dispersed phase* and which the *continuous phase* (dispersion medium)—is also determined by the nature of the emulsifying agent. If one part of the adsorbed molecule is larger in diameter than another part, the whole molecule will have somewhat the shape of a wedge or cone, and the form of the emulsion will be determined by the orientation of these "wedge-shaped" molecules in the phase boundary surface (Fig. 18). Thus, if the polar part of the molecule is larger in diameter than the nonpolar part, the broader end will be in the water phase and the narrower end in the oil phase; the packing together of such molecules at the interface will then obviously cause this surface to be curved, with the broader ends of the molecules outward: that is, the oil (nonpolar) phase will be forced to assume the form of drops surrounded by water (Fig. 18, *A*). If, on the other hand, the nonpolar part of the adsorbed molecules is broader, the water must assume the form of drops dispersed in the oil. Sodium or potassium soaps form oil-in-water emulsions, while calcium or magnesium soaps form water-in-oil emulsions. In a sodium soap, one fatty acid radical is combined with each sodium ion; the latter is larger in diameter, and the broader end of the "wedge" is therefore in the water, the narrower end in the oil phase. In a calcium soap, however, two fatty acid

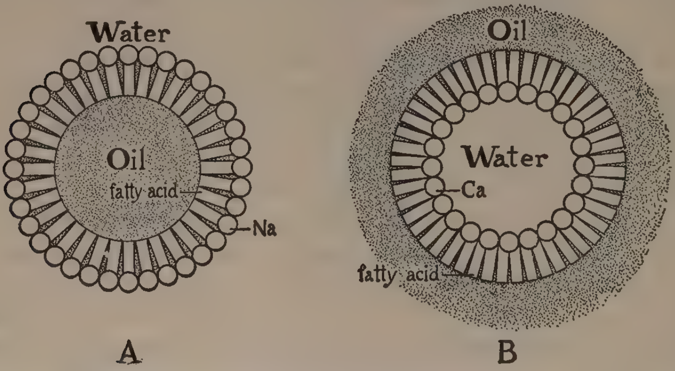


Fig. 18.—Diagrams to illustrate the theory of emulsification. *A*, an oil-in-water emulsion, with a sodium soap as emulsifying agent; *B*, a water-in-oil emulsion, with a calcium soap as emulsifying agent.

radicals are combined with each calcium ion; the nonpolar end of the molecule, in the oil phase, is therefore the broader end (Fig. 18, *B*). The form of such emulsions can be changed by altering the ratio of sodium and calcium ions in the solution; this is called *phase reversal* (Fig. 19).

An emulsion consisting of relatively little oil and a larger amount of water is more viscous when in the form of a water-in-oil emulsion than when in the form of an oil-in-water emulsion. If the continuous phase is relatively small in amount, most of it will be in the form of surface films surrounding the drops of the dispersed phase; this may give the whole emulsion the consistency of a gel (p. 71).

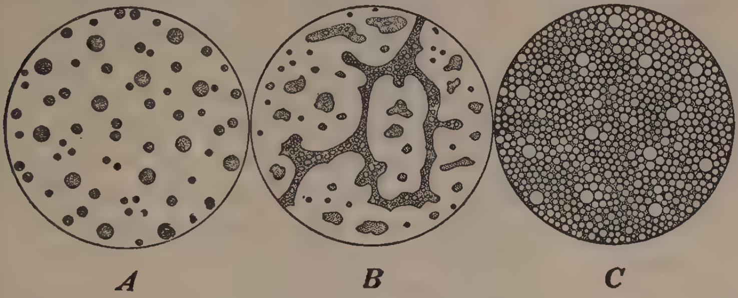


FIG. 19.—Phase reversal in an emulsion, as seen with the microscope; the oil contains a dye to make it darker. *A*, oil-in-water emulsion, with a sodium soap as emulsifying agent. *B*, a calcium salt has been added gradually until, at a certain critical ratio of calcium to sodium ions, the emulsion "breaks," as shown in this drawing; this state is very unstable, the two phases being in continual rapid motion and rearrangement. *C*, after a further addition of calcium ions, the mixture assumes the form of a water-in-oil emulsion, of this appearance.

In protoplasm, there is a great deal more water than lipins. The viscosity of protoplasm is therefore determined in part by the relations of these two kinds of phases. This may differ in different cells, in different parts of the same cell, and in the same part under different conditions. The form of the emulsion will depend on the local and momentary concentrations of the various substances which act as emulsifying agents. These, in turn, are affected by chemical changes both within the cell and in the surrounding fluids; *e.g.*, changes in the ratio of sodium and calcium ions. Other important properties of protoplasm, besides its viscosity, may be affected by these phase relations, and therefore by any factors which alter these.

Colloidal dispersions include, as we have seen, both true solutions with relatively large solute molecules and suspensions or emulsions with relatively small multi-molecular particles. These two types of colloidal dispersions overlap not only in the size of their dispersed particles (p. 62) but also in other properties, so that no sharp distinctions can be drawn between them. The stability and many other properties of a colloidal dispersion depend chiefly on the degree of *hydration* of the dispersed particles. All the colloids of biological importance are of the heavily hydrated type, which are called *hydrophile* colloids (as contrasted with *hydrophobe* colloids, such as colloidal suspensions of metals and other inorganic substances). The properties of hydrophile colloidal dispersions, whether their dispersed particles consist of single or many molecules, are in many respects more like those of solutions than like those of typical suspensions or emulsions. They differ from crystalloidal solutions, however, in several respects, due chiefly to the larger size of their molecules or particles: the dispersed substance diffuses very slowly and does not pass through a dialyzing membrane (p. 63); the dispersions appear cloudy (p. 60); they are usually more viscous than crystalloidal solutions, and often "set" to form gels (p. 71). Some other special properties of these colloidal dispersions depend on the chemical nature of their components, which are usually complex substances of the polar-nonpolar type.

Among the important components of protoplasm which are in the colloidal state are proteins, lipins, and polysaccharoses. Some of these are chiefly in true solution, others in suspension or emulsion, the degree of dispersion or aggregation of the individual molecules depending both on their own chemical constitution and on various conditions in the dispersion medium. The proteins and phospholipins are electrolytes, while the other lipins and the carbohydrates are non-electrolytes.

Proteins, as previously explained (p. 52), ionize both as acids and as bases, and form salts with inorganic ions. Since each protein molecule contains many acid and basic radicals, these salts consist of many small inorganic ions associated with relatively few large protein ions. Like other salts, they are highly ionized in solution. The inorganic ions, although themselves of crystalloidal dimensions, are prevented from diffusing freely by the electrostatic attraction of the oppositely charged protein ions. This phenomenon plays a large part in the complex behavior of protein solutions and suspensions, and in many activities of the living cell. The phospholipins also have free acid and basic groups (see formula on page 50), and therefore behave much like the proteins in this respect. Since most of the proteins and phospholipins are somewhat more strongly acidic than basic, they exist in protoplasm chiefly as anions or negatively charged particles, associated with inorganic cations, principally potassium, which is the most abundant cation in cells.

Gels.—In many colloidal solutions, the colloidal molecules have a tendency to cling together, forming network-like aggregates. This is due partly to the large size and consequent relatively slow Brownian movement (p. 62) of these molecules, and partly to their chemical constitution. In polar-nonpolar molecules, the nonpolar groups, having no affinity for water, tend to stick together, while the polar groups, with a strong affinity for water, prevent the substance from being precipitated or "squeezed out." It will be noted that these factors involved in the formation of molecular aggregates in colloidal dispersions are the same as those involved in surface-activity (p. 66). When there is a sufficient proportion of such a substance in the dispersion, and the temperature is sufficiently low (so that Brownian movement is not too rapid), this network-like structure may extend throughout the whole volume of the dispersion and hold the water in its meshes, so that the whole system behaves as a solid: this is called a *gel* (Fig. 20).

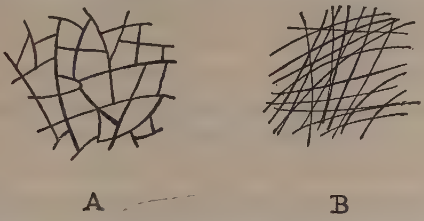


FIG. 20.—Diagrams of the ultramicroscopic structure of gels. *A* represents the structure of a very firm gel, *B* that of a softer gel. The black lines represent the solid phase, the white spaces the liquid phase.

A dispersion of such a substance (*e.g.*, gelatin) in water passes gradually, as the temperature is lowered, from the condition of a true solution (separate molecules) through that of an emulsion or suspension (molecular aggregates) to that of a gel, with continuously increasing viscosity. In a completely solidified gel, both phases, solid and liquid, are continuous (Fig. 20, *A*). The network-like structure of the solid phase gives solidity—*i.e.*, rigidity and elasticity—to the gel, while water and crystalloid solutes, with small molecules, are able to diffuse freely through it between the meshes of this network. A considerable proportion of the water is combined with the polar groups of the gel-forming substance, as water of hydration, and the rest of the water is held in the interstices of the network by cohesion. Thus a relatively small proportion of a substance such as gelatin may hold a much larger amount of water in such a way that the whole system forms a solid, fairly rigid, gel.

Many of the colloidal components of protoplasm—proteins, phospholipins, and polysaccharoses—have the ability to form gels. The gelation and liquefaction of these substances are affected not only by temperature but also by other conditions of the medium, especially by various inorganic ions which affect the hydration and the aggregation of the colloidal molecules. These factors play a large part in the structure of protoplasm and in the mechanism of protoplasmic movements (Chapter XIV).

The structure of protoplasm.—Protoplasm is a dispersion of many substances in many conditions. The dispersed particles range in size from the smallest inorganic molecules and ions to microscopically visible formed bodies, with a perfectly continuous gradation between these extremes. In chemical nature they range from highly polar substances such as salts, very soluble in water, to nonpolar substances such as fats and sterols, quite insoluble in water. Protoplasm is therefore a heterogeneous mixture of many phases, liquid and solid; each phase being itself a complex solution of many substances and bounded by a surface film in which various substances are adsorbed (p. 67).

This structure differs in detail in different cells, in different parts of a cell, and under different conditions. The cytoplasmic ground substance in the interior (endoplasm) of many cells seems to be an aqueous fluid; *i.e.*, a dispersion in which water is the continuous phase. The free surfaces of protoplasm—*e.g.*, the plasma membrane, vacuolar membranes, etc.—seem, however, to have the properties of an emulsion in which lipin is the continuous phase (p. 88). The more solid bodies, such as chromosomes, plastids, and fibrils, and the firm outer layer (ectoplasm) of many cells, probably have the structure of gels. At times the whole cell, or most of it, has the consistency of a gel. Changes from fluid to solid consistency, and vice versa, often occur quite rapidly in the living cell; these may be due to gelation and liquefaction of gel-forming substances (p. 72), or to phase reversals of emulsions (p. 69). These structural changes are brought about by chemical changes within the cell or in its external environment, such as changes in the concentrations of H+, OH−, and other ions. Changes of this kind probably play an important part in the mechanism of protoplasmic movements (Chapter XIV).

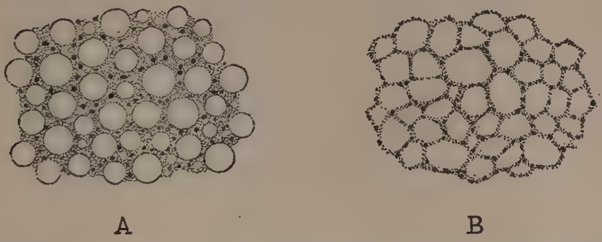


FIG. 21.—*A*, protoplasm of a starfish egg, in the living condition, showing alveolar and granular structure; *B*, the same killed and fixed, showing reticular structure. (Adapted, in part, from Wilson.)

The microscopic appearance of protoplasm, aside from the definite formed bodies (p. 25), may be alveolar (Fig. 21, *A*), granular, or perfectly homogeneous. Even when it appears homogeneous under the microscope, however, ultramicroscopic examination shows it to be full of colloidal particles. The differences between these different microscopic appearances of protoplasm in different cells are essentially merely differences in the size of the dispersed particles. The "alveolar" structure is that of a relatively coarse emulsion. The "granular" appearance in other cases is due to the dispersed particles being smaller, at the very limit of microscopic visibility, and relatively further apart. When these particles are still smaller they are invisible with the ordinary microscope, but show up under the ultramicroscope (Fig. 16). When cells have been killed and fixed (p. 18), the dead "protoplasm" commonly has a reticular structure (Fig. 21, *B*), like the structure of a gel (Fig. 20) but on a much coarser, microscopic, scale. This structure varies with the kind of fixative employed; it is produced by the coagulation (irreversible gelation) of the organic components, such as proteins, and the precipitation of some of the dissolved substances.

The structure of living protoplasm has only begun to be studied by physico-chemical methods within very recent years, and there is still a great deal to be learned about it. One of the most certain conclusions, perhaps, that can be drawn from our present knowledge of this subject is that there is no one definite universal structure of protoplasm, but that it is heterogeneous, diverse, and changeable. We shall see in later chapters that the differences of protoplasmic structure in different kinds of cells and different parts of the cell, and the changes of this structure under different conditions, are of great importance in the activities of the living organism.

CHAPTER V

EXCHANGES BETWEEN THE CELL AND ITS ENVIRONMENT: DIFFUSION, OSMOSIS, PERMEABILITY

THE series of chemical changes within the living cell, upon which its life depends, requires a continuous supply from without of food substances, and the continuous removal of its waste products. The exchanges of materials between the living cell and its environment are therefore of utmost importance to the life processes. Some kinds of cells can ingest and egest solid particles (Chapters VII, XII); but in the great majority of cases, the substances which enter and leave the cell do so in the *dissolved* state. The processes by which dissolved substances get into and out of living cells will be discussed in the present chapter.

Diffusion.—If any substance be dissolved in one region of a body of liquid, it will spread gradually until it is evenly distributed throughout the whole volume of the liquid. This process is called *diffusion*. Its cause is the random movements of the solute molecules, which we recognize in the case of visible particles as Brownian movement (p. 62), and which is a manifestation of the molecular kinetic energy, or heat, present in all substances. These movements, being entirely random (*i.e.*, in all directions, determined only by the chance collisions among solute and solvent molecules), must result eventually in the equal distribution, throughout the whole solution, of every kind of molecule (solvent and solute) present in it. It is evident, therefore, that any substance present originally in greater concentration in one region of the solution will diffuse from this region to those where it is less concentrated. The diffusion of a solute from its original place of solution to other parts of the liquid implies, of course, the diffusion of the solvent in the opposite direction; *i.e.*, from the regions where it (the solvent) is more concentrated to that where it is less concentrated. We may state as the general law of diffusion: in any continuous body of fluid every component substance will diffuse from the regions of its greater concentration to the regions of its smaller concentration, until every substance present is equally concentrated throughout.

The process of diffusion is very slow, for distances visible with the naked eye; but within microscopic and ultramicroscopic distances the equalization of concentrations may take place very quickly. The *rate of diffusion* depends on several factors: size of the diffusing molecules, temperature, concentration of the diffusing substance, and nature of the medium through which it is diffusing. The velocity of Brownian movement of a molecule or particle depends on its size and on temperature (p. 62) and the rate of diffusion is therefore affected in the same way by these factors; *i.e.*, larger molecules diffuse more slowly than smaller ones, and the rate of diffusion increases with rising temperature. The rate of diffusion also varies with the *concentration* of the diffusing substance; *i.e.*, the number of molecules of this substance per unit volume of solution. Other things being equal, the rate of diffusion between two points is proportional to the *difference* in the concentrations of the diffusing substance at these two points. The nature of the medium through which a substance is diffusing also greatly affects its rate of diffusion: greater viscosity (internal friction) of the solvent will obviously tend to retard the diffusion of dispersed particles. The *structure* of the diffusion medium, in case this be a *gel*, a *porous solid*, or an *emulsion*, is particularly important. Thus a gel (*e.g.*, gelatin) which has a network-like structure (p. 71) offers very little impediment to the diffusion of crystalloidal molecules, which are small enough to pass easily between its meshes; but it may block entirely the diffusion of colloidal molecules or particles, which are too large to do so. The same is true of a solid *membrane* with ultramicroscopic pores, which has essentially the same structure as a gel; namely, a two-phase, solid-liquid, system in which both phases are continuous. If the diffusion medium be an emulsion, a substance which is soluble in both phases will diffuse through it more rapidly than one soluble in only the continuous phase; while a substance soluble in only the dispersed phase can scarcely diffuse through the emulsion at all. There are thus two important factors (aside from temperature, concentration, etc.) determining the possibility and rate of diffusion through such two-phase systems (gels, membranes, emulsions); namely, the size of the diffusing molecules or particles, and their solubility in both phases of the diffusion medium.

Semi-permeable membranes.—If two solutions differing in composition or concentration be separated by a membrane freely permeable to all their components, these will, of course, diffuse through this membrane until the two solutions become identical, just as though no membrane were present. But there are many kinds of membranes which are permeable to some liquids and dissolved substances, but impermeable, or less permeable, to others; such membranes are called, in general, *semi-permeable membranes*. This differential permeability to different substances may be due, as already noted, either to the different sizes of the molecules of these substances, in relation to the size of the ultramicroscopic pores (inter-molecular spaces) of the membrane, or to their different solubilities in the substance of which the membrane is composed. Thus, many membranes (*e.g.*, parchment, collodion, and many dead plant and animal tissues) are quite freely permeable to water and crystalloidal solutes, but impermeable to colloids; this is probably due to the greater size of the colloidal molecules or particles, which are too large to pass through the ultramicroscopic pores of these membranes. On the other hand, a rubber membrane is impermeable to water, but permeable to ether; in this case, the relative size of the molecules has probably nothing to do with it; ether is soluble in rubber (an organic substance), while water is not. Similarly, a membrane of any fatty substance would be permeable to fat-soluble (nonpolar) substances, but impermeable to non-fat-soluble (polar) substances. This is, to a considerable extent, true of the living plasma membrane of cells (p. 86).

The differences in permeability of a semi-permeable membrane to different substances are often really differences in *degree* of permeability—*i.e.*, in the rates of diffusion of these different substances through it—rather than free permeability to some and complete impermeability to others. Thus, while a dialyzing membrane (*e.g.*, parchment) is permeable to crystalloidal solutes such as salts and sugars, these do not diffuse through it nearly as rapidly as water does; on the other hand, some colloidal substances, such as starch and proteins, to which the membrane is "impermeable," may be found to have diffused through it to a slight extent after a long time. Similarly, the living plasma membrane is not entirely impermeable to polar solutes, such as sugars and amino-acids, but these diffuse through it much more slowly than fat-soluble substances (p. 86).

Osmosis.—If two different solutions be separated by a semi-permeable membrane, impermeable to some of their components but permeable to others, the latter will diffuse through the membrane until the two solutions become identical in composition and concentration, provided no other force prevents this (p. 79). This process, diffusion through a semi-permeable membrane, is called *osmosis*. Since all the cell membranes (p. 27), and the cells and tissues themselves, are semi-permeable membranes, it is by osmosis that all liquids, gases, and dissolved substances enter and leave the cells and body-fluids of organisms; it is therefore of the utmost importance in life processes.

In osmosis, as in any other case of diffusion, the direction of diffusion of any substance which can diffuse at all must be from the region of its greater concentration to that of its lesser concentration. Thus, if a sugar solution be separated from pure water by a parchment membrane (which is permeable to sugar), sugar will diffuse through this membrane until its concentration is equal on both sides; similarly, if a stronger and a weaker sugar solution be separated by such a membrane, sugar will diffuse from the former to the latter. In case the diffusing substance is the solvent (*e.g.*, water) it also will diffuse from the region where it is more concentrated to that where it is less concentrated; *i.e.*, from the weaker solution (containing less solute, and therefore relatively more solvent) to the stronger solution (containing more solute, and therefore relatively less solvent). Thus, if a stronger and a weaker sugar solution be separated by a membrane of copper ferrocyanide (which is permeable to water, but impermeable to sugar), water will diffuse from the weaker sugar solution to the stronger one until the two are equally concentrated, if conditions be so arranged as to permit this (p. 80). In case a sugar solution be separated from pure water by such a membrane, the two could never become equally concentrated since the one contains no sugar at all; in this case all the water would eventually diffuse into the sugar solution, if possible.

The cause of this unequal diffusion of the solvent through a membrane impermeable to the solute may be pictured thus: Suppose a sugar solution which contains 1 sugar molecule to every 100 water molecules separated from pure water by a semi-permeable membrane impermeable to sugar. A certain very small volume of this sugar solution would contain 100 water molecules and 1 sugar molecule, while an equal volume of the pure water would contain 101 water molecules. A certain very small area of the semi-permeable membrane would, then, be struck, on the side toward the sugar solution, by 100 water molecules and 1 sugar molecule in, say, one second; but on the other side, in

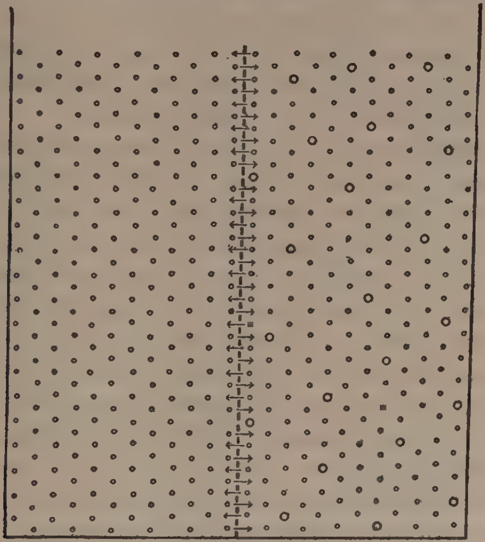


FIG. 22.—Diagram to illustrate the theory of osmosis. The smaller circles represent water molecules, the larger circles sugar molecules; the perforated line represents a semi-permeable membrane permeable to water but impermeable to sugar. It is evident that, under the conditions here represented, more water molecules will pass through the membrane from left to right than in the opposite direction.

the same second, by 101 water molecules. The water molecules could pass through it, the sugar molecule could not; therefore 101 water molecules would pass through in one direction (from the pure water to the sugar solution) while only 100 passed through in the opposite direction; *i.e.*, water would diffuse through 1% faster into the sugar solution than from it (Fig. 22). No matter how small this difference in rate of diffusion in the two directions, it must result in an increase of the amount of water in the sugar solution, and this must continue until the two solutions are identical in concentration or, in the case we have supposed, until the water has all passed into the sugar solution, unless some other force operates to prevent this.

Osmotic pressure.—In practice, the conditions necessary to permit equalization of two solutions, separated by a membrane permeable only to the solvent, are seldom realized; another force does practically always operate to prevent this. Let us suppose, first, that the stronger solution (containing more solute) is *completely enclosed* in a vessel with rigid walls; then the entrance of more water into this solution, by osmosis, will very quickly develop a pressure within the containing vessel which will prevent the entrance of any more water. If we suppose the containing vessel to be less rigid, then it will swell until its resistance to further distension develops sufficient pressure to prevent the entrance of any more water—unless, of course, the vessel bursts. If the containing vessel be open at the top (as in Fig. 22) or incompletely filled with the solution, the entrance of more water by osmosis will increase the volume of this solution and raise its level, while the level of the weaker solution, or pure solvent, in the adjoining vessel will fall, until this difference in level of the two liquids develops sufficient pressure (weight of the liquid above the lower level) to prevent the entrance of any more water into the liquid with the higher level.

In all these cases, we see, the faster diffusion of the solvent into the stronger solution results in a pressure in that solution which finally stops the process. This pressure is called *osmotic pressure*. The amount of this pressure can be measured by the distension of the containing closed vessel, or by the rise in level of the solution in an open vessel. The osmotic pressure of a solution is defined as the pressure necessary to just prevent any increase in its volume by osmosis, when it is separated from the pure solvent by a semi-permeable membrane impermeable to the solute. Since the cause of the unequal diffusion which produces this pressure is the excess of solvent molecules in the pure solvent, as compared with an equal volume of the solution, and since this excess is equal to the concentration (number of molecules per unit volume) of the solute in the solution, the osmotic pressure of any solution is proportional to the *molecular concentration* of its solute; *i.e.*, it depends only on the *number* of solute molecules in a unit volume of the solution, not on their composition or properties. In the case of electrolytes, however, it should be noted that each molecule, in the chemical sense, splits into two or more ions in solution; each of these ions then acts as a separate molecule in determining the osmotic pressure; electrolytes therefore give much higher osmotic pressures, for the same number of chemical molecules, than non-electrolytes. It must be borne in mind, also, that substances with larger (heavier) molecules will have fewer molecules, and therefore smaller osmotic pressures, for the same concentration *by weight*, than substances with smaller molecules. Thus colloids, *e.g.*, starch, with very large molecules, give very small osmotic pressures, even in very concentrated solutions by weight. In the case of colloids which are also electrolytes, *e.g.*, proteins, however, the osmotic pressure is determined chiefly by the many small (inorganic) ions associated with them (p. 70) rather than by the relatively few large colloidal ions; they therefore give much higher osmotic pressures, for the same concentration by weight, than non-electrolytic colloids. For these reasons, the osmotic pressure of cells and body-fluids of most organisms is determined principally by their inorganic salts and their proteins; sugars are also an important factor in some plant cells (p. 173).

Osmosis and osmotic pressure in living cells.—The plasma membrane which surrounds the protoplasm of every living cell (p. 27) is a semi-permeable membrane, fairly permeable to water but much less permeable to many dissolved substances, such as salts and sugars. This membrane is also fairly tough, distensible, and elastic. The living cell acts, therefore, as a solution (of salts, proteins, etc.) surrounded by a continuous, semi-permeable and somewhat distensible membrane. When immersed in water, or in salt or sugar solutions, osmosis (of water) occurs between the inside of the cell and this external liquid. The direction of osmotic flow (greater rate of diffusion of water) is, of course, always from the solution containing the greater concentration *of water* (*i.e.*, the smaller concentration of solute molecules), whether this be the cell or the external medium. Since only the number of solute molecules, not their kind, determines the osmotic pressure of a solution, any solution containing the same number of solute molecules per unit volume as the interior of the cell, will have the same osmotic pressure as the cell, regardless of the kind of solute, provided it is one to which the plasma membrane is impermeable (under the given conditions). Such a solution is called *isotonic* to the cell. A solution more concentrated, in this sense (*i.e.*, containing a greater number of indiffusible solute molecules per unit volume), than the interior of the cell is called *hypertonic;* one less concentrated *hypotonic.*

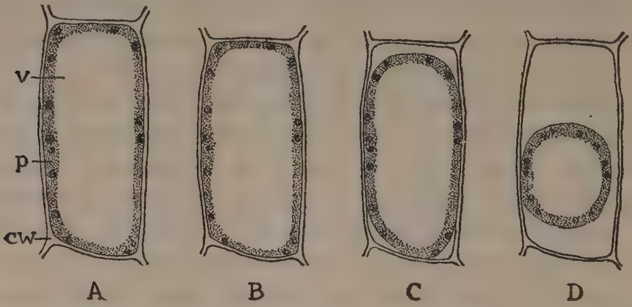


FIG. 23—Plasmolysis. *A*, a living plant cell in water; *v*, vacuole; *p*, protoplasm; *cw*, cell wall. *B*, the same cell in 4% potassium nitrate solution; *C*, in 6% solution; *D*, in 10% solution. (After De Vries.) In the normal condition (*A*) the cell wall is somewhat stretched by the outward pressure of the cell; when this pressure is removed, by plasmolysis, the elasticity of the wall results in its slight shrinkage (*B*, *C*, *D*).

If a living cell be immersed in a hypertonic solution of any substance to which it is impermeable, water must diffuse out of the cell more rapidly than into it, since the interior of the cell contains relatively fewer solute, and therefore relatively more water, molecules. The cell, therefore, will decrease in volume, *i.e.*, shrink. In the case of plant cells, which are surrounded by a cellulose cell wall, the cell itself (*i.e.*, the protoplasm, with its plasma membrane) shrinks away from the more rigid cell wall, leaving a space between them; this is called *plasmolysis* (Fig. 23). In animal cells with a less rigid cell membrane, this usually adheres to the cell and often becomes wrinkled as the cell shrinks; this is called *crenation* (Fig. 24). Plasmolyzed or crenated cells can be restored to their normal size and form by replacing them in an isotonic solution. If the solute of a hypertonic solution can diffuse into the cell, but less rapidly than water, the cell will be plasmolyzed, or crenated, temporarily, but will eventually regain its normal size when enough of this solute has entered it to equalize the osmotic pressures inside and outside; this occurs with hypertonic solutions of glycerol, etc., and also, but much more slowly, with some salts and sugars. A solution of a substance which diffuses into the cell as rapidly or more rapidly than water (*e.g.*, alcohol) can never plasmolyze or crenate the cell, no matter how concentrated.

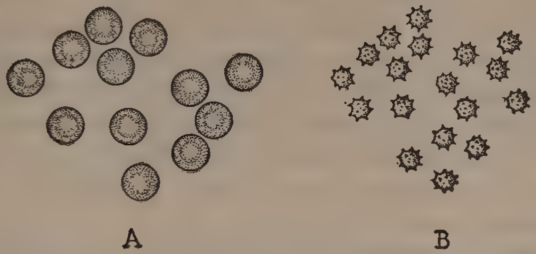


FIG. 24.—Crenation of red blood corpuscles. *A*, normal form, in isotonic solution; *B*, shrunken and crenated, in hypertonic solution.

If the cell be placed in a hypotonic solution, water must diffuse inward more rapidly than outward; hence the cell will tend to swell. In a plant cell, this is impossible because of the rigid cell wall surrounding it; hence there is little or no visible change in a hypotonic solution. But animal cells, without a rigid cell wall, actually swell in such solutions and may finally burst; this is called *cytolysis*. However, the outer membrane surrounding most animal cells, and even the plasma membrane itself, have a certain amount of toughness which resists this swelling and bursting, so that the external solution must be considerably hypotonic to the cell in order to actually burst it. Thus, human blood corpuscles, which are actually isotonic with a 0.9% sodium chloride solution, do not burst in a hypotonic solution until it has been diluted to about half this concentration (*i.e.*, about 0.45% NaCl). So long as they have not actually burst, these swollen cells can be restored to their normal size and form by replacing them in an isotonic solution.

In an isotonic solution, of course, the cell neither shrinks nor swells. This fact can be used to determine what solutions are actually isotonic with the cell: a solution which causes neither shrinking nor swelling (of animal cells), or which just fails to plasmolyze (plant cells), is judged to be isotonic with the cell. In this way, we can determine the osmotic pressure of the cell itself, which must be equal to that of an isotonic solution of known osmotic pressure; or, conversely, knowing the osmotic pressure of the cell, we can by this method determine the osmotic pressure of a solution isotonic with it.

The osmotic pressure of the living cells is very different in different organisms; it is usually equal to, or slightly greater than, that of the fluids by which the cells are normally surrounded. Many marine organisms have an osmotic pressure in their cells and body-fluids about equal to that of the sea water; this is quite variable, in different parts of the oceans and coast waters, and the internal osmotic pressure of these organisms varies with it; an average value, for salt water near the coast, is isotonic with (approximately) a 25% solution of sucrose or a 3% solution of sodium chloride. Fresh-water organisms have internal osmotic pressures much less than this; *e.g.*, the cells of Spirogyra, a simple fresh-water plant (Fig. 14), are isotonic with a 6% solution of sucrose or a 0.6% solution of sodium chloride; but this is considerably greater than the osmotic pressure of the water in which they live. Thus fresh-water organisms really live in a hypotonic solution; in the case of plants, the cells are prevented from swelling by the cell walls; fresh-water animals, both unicellular and multicellular, have special mechanisms (Chapters VII, XII) which constantly eliminate the excess water which enters by osmosis. The higher animals have an osmotic pressure in their cells about equal to that of their body-fluids (blood, etc.), which is kept very constant by the action of special organs, the *kidneys* (Chapter XII); the blood of man, for instance, is isotonic with a 10% solution of sucrose or a 0.9% solution of sodium chloride.

Plant cells in general, and the tissue cells of higher animals, have osmotic pressures at least slightly greater than those of their surrounding fluids, because of the greater concentration of proteins within the cells. These cells are prevented from actually swelling by their surrounding walls and membranes and especially by their close packing together in the tissues. Their tendency to swell by inward osmosis of water, however, results in rigidity, like that of a tightly inflated balloon; this is called *turgor*. This turgor is responsible for the maintenance of form and rigidity in tissues and organs without hard parts. It is illustrated by the normal state of a living leaf as contrasted with a wilted leaf. If the leaf be placed in a hypertonic solution (of, *e.g.*, salt or sugar), it will wilt, because the cells lose water by osmosis; turgor can be restored by replacing the leaf in an isotonic or hypotonic solution. Leaves also wilt when they have insufficient moisture, because of the loss of water from the cells by evaporation; in this case also turgor can be restored by supplying sufficient water. If the leaf be killed (as by heat, poisons, etc.), it also wilts; in this case because the plasma membrane of the cells is destroyed, and many of the dissolved substances within the cells diffuse out, thus decreasing the osmotic pressure, and therefore the turgor, of the cells; in this case, of course, turgor can not be restored.

Permeability of living cells.—The permeability of living cells to dissolved substances (*i.e.*, the ability of such substances to diffuse into and out of the cells) is very complex and variable: it differs with the kind of cell, the nature of the diffusing substance, and various internal and external conditions. In general cells are impermeable to colloidal substances, such as proteins and polysaccharoses; this is true not only of the living cells, but also of dead cells and tissues. Membranes composed of dead cells (*e.g.*, bladder, gut, etc.) are generally permeable to crystalloidal solutes; *i.e.*, they act as dialyzing membranes (p. 63). This is, however, not true of *living* cells, which show great differences in permeability to various kinds of crystalloidal solutes.

Generally speaking, the living cell is more permeable to *nonpolar* than to *polar* substances; the more highly polar a substance is, the less readily it passes into or out of the cell. There are, however, many other factors entering into the matter, which often obscure or apparently contradict this general rule.

All cells are freely permeable to dissolved gases, such as oxygen, carbon dioxide, and ammonia; and also to predominantly nonpolar organic compounds, especially those with relatively small molecules, such as ether, chloroform, etc. Most cells are permeable to water, but this penetrates more slowly than many organic compounds. Sugars and amino-acids seem to enter very slowly, though all cells must certainly be permeable to them to some extent, for these are essential food substances of all cells. Many kinds of cells seem to be very impermeable to inorganic salts, though this differs greatly with different kinds of cells and with different salts. That these substances do get into the cells in some way is proved by the fact that all cells contain certain of these salts (p. 42), but the conditions under which they enter are still very imperfectly understood.

Changes in permeability.—Not only do different kinds of cells differ in their permeability to dissolved substances, especially to water-soluble crystalloids, but the permeability of any particular cell changes according to various conditions within the cell or in the external medium. Among the most striking effects of external factors are those of inorganic ions, especially cations. Cations with one charge (K^+, Na^+, etc.) generally increase, while those with more than one charge (Ca^{++}, Mg^{++}, etc.) generally decrease, the permeability. A "balanced solution," containing sodium and calcium ions in the ratio of 100 Na^+ to 1 or 2 Ca^{++} (the ratio in which they occur in sea water and most body-fluids of animals) maintains the normal permeability of the cell unchanged, for some time at least; but to keep the cell perfectly normal and healthy indefinitely usually requires the presence of three or all four of these cations (K^+, Na^+, Ca^{++}, Mg^{++}) in the surrounding fluid. Such a solution, containing all the necessary ions in the proper ratios, and isotonic with the cell, is called a "physiological salt solution." Anions generally work in the opposite way;

i.e., those with more than one charge increase cell permeability more than those with a single charge; but their effects are usually much less marked than those of cations. Hydrogen and hydroxyl ions are exceptions to both these rules: hydrogen ions generally decrease, while hydroxyl ions increase, permeability. All of these ions, if sufficiently concentrated, or if the cell is exposed long enough to them in "unbalanced" solutions, may kill or permanently injure the cell, whose permeability then always increases.

Another class of substances which decrease permeability markedly are *anaesthetics:* alcohol, ether, chloroform, etc. In moderate concentrations, they decrease the permeability of the cell; in greater concentrations, or acting for a longer time, they may kill the cell, whose permeability then increases. In a later chapter we shall see that there are also changes in permeability caused by processes within the cell itself, which are an essential part of some of its normal activities (Chapter XIII).

It has been mentioned above that dead cells are much more permeable than living ones to water-soluble crystalloidal substances. When the cell is killed, not only can such substances enter it freely from outside, but its own crystalloidal components (salts, sugars, etc.) diffuse out; the internal osmotic pressure therefore decreases, the cell loses its turgor and collapses; dead tissues thus become limp. The escape from the dead cells of dissolved substances which are retained by the living cells is easily seen in tissues with colored cell-sap, such as a red beet: if this be killed (by heat or poison), the red pigment, which does not escape from the living cells, exudes freely; the sugar and salts do so also. If cells are injured in any way, their permeability also increases; if the cell recovers from the injury its permeability returns to normal, if the injury is permanent it does not; if the permeability reaches the point of complete permeability to water-soluble crystalloids, the cell never recovers—it is dead. The permeability of cells is thus a means of measuring injury, recovery, and death.

Structure of the plasma membrane.—The peculiarities of permeability of the living cell are not due to the cell walls or external, non-living, cell membranes, for these are, in general, permeable to all crystalloidal solutes. Nor can these phenomena be ascribed primarily to the internal protoplasm of the cell, for many dissolved substances which will not permeate the cell from outside will nevertheless, when *injected* into the interior of the cell, diffuse throughout the cytoplasm but *not* through the plasma membrane, vacuolar membranes, or nuclear membrane. The permeability of the living cell to such substances—water-soluble crystalloids—and its changes of permeability must, then, be explained by the composition and structure of the *plasma membrane*, or surface film of the protoplasm.

The fact that living cells are, in general, more permeable to lipin-soluble (nonpolar) than to water-soluble (polar) substances suggests that the plasma membrane is predominantly lipin in composition. Many of the facts of cell permeability and its changes can be explained by conceiving the plasma membrane as a colloidal emulsion of aqueous and lipin phases, of which the lipin is ordinarily the continuous phase. Substances, such as gases, soluble in both phases can of course diffuse through such a membrane freely at all times. Lipin-soluble (nonpolar) substances can also penetrate it freely; since the lipin phase is continuous and affords them a through passage (Fig. 25, *A*). Water-soluble (polar) substances, on the other hand, can not pass through it freely, since they can not diffuse from one to another of the dispersed water droplets. Many such substances, however, as we have seen, do penetrate slowly, and water itself penetrates fairly rapidly in most cases. To explain this, we must bear in mind that the plasma membrane is part of the *living* protoplasm, and as such is not a fixed, stable structure, but in constant movement and change; the dispersed water droplets must be continually coalescing and breaking up again; in this way water and substances dissolved in

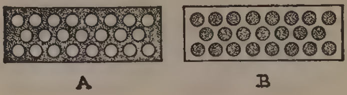


FIG. 25.—Diagrams to illustrate the theory of cell permeability. *A*, the usual normal condition of the plasma membrane: lipin phase continuous, aqueous phase discontinuous; in this condition, lipin-soluble substances can obviously pass through more freely than water-soluble substances. *B*, the phases reversed, aqueous phase now continuous; in this condition water-soluble substances can pass through more freely than lipin-soluble substances.

it would gradually work their way through this membrane. Moreover, the lipin phase is probably largely composed of phospholipins, since these are the most abundant lipins in most cells (p. 50), and these substances, unlike other lipins, are permeable to water.

The changes in permeability by which the plasma membrane becomes more permeable to water-soluble substances must involve a phase reversal by which this water-in-oil type of emulsion is changed, more or less, to an oil-in-water type (p. 69). This would permit the free diffusion of water-soluble molecules sufficiently small to pass between the lipin droplets; but not of colloidal molecules which are too large to do so (Fig. 25, *B*). We have seen that certain ions (Na^+ and K^+) which increase cell permeability actually do affect emulsions in this way, while those (Ca^{++} and Mg^{++}) which decrease permeability have the opposite effect (p. 68). Many of the substances and conditions which change the permeability of cells, one way or the other, may do so by such effects on the phase relations of the water-lipin emulsion. Other components of the plasma membrane, such as proteins, may also play some part in these phenomena.

The plasma membrane has a degree of toughness and elasticity which implies some kind of solid structure, and there is other evidence which indicates that it contains protein. We may conceive this elastic structure as being a gel, or network-like structure, of protein, in the interstices of which is an emulsion such as described above; or the plasma membrane may consist of two layers, one composed largely of protein, giving it toughness and elasticity, the other largely lipin, controlling its permeability. The whole thickness of the plasma membrane is ultramicroscopic, so that it can not contain more than a few layers, at most, of large molecules like those of proteins or phospholipins.

The effects of injury and death on cell permeability indicate that under these conditions the structure of the plasma membrane breaks down in such a way that the water phase becomes continuous, thus making the cell freely permeable to water-soluble crystalloids. The fact that the characteristic semi-permeable properties of the plasma membrane are retained only so long as the cell is alive (metabolizing) shows that its structure is not stable, *i.e.*, will not "stay put" by itself, but can only be maintained by a constant expenditure of energy.

Intracellular membranes.—At every surface of contact of a liquid with another phase—gas, solid, or another liquid—there exists a surface film (p. 64). Certain kinds of dissolved substances—surface-active substances—accumulate in these surface films, with their molecules oriented in definite ways depending on the composition of each phase (p. 66). Protoplasm, as we have seen, is a system of many phases, and contains many surface-active substances—lipins, proteins, etc. Therefore at every phase-boundary within the protoplasm, as well as at its surfaces of contact with other materials (external fluids, cell-sap in vacuoles, etc.) there must exist a surface film, or membrane, composed chiefly of surface-active substances with definite molecular orientations. Every such phase-boundary film is really a joint product of the two phases which it separates, its composition and structure being determined by both of them; its properties will therefore vary with changes in either of these phases.

The plasma membrane is a film of this nature, formed at the surface of contact of protoplasm with external fluids (water or body-fluids); its properties, as we have seen above, differ in different kinds of cells and vary with changes in either the cell or the external medium. A similar membrane surrounds every vacuole within the cell; the properties (permeability, etc.) of these *vacuolar membranes* are, in general, like those of the plasma membrane and vary in the same ways. The *nuclear membrane*, separating the nucleus and cytoplasm during the growth ("resting") stage, is usually even less permeable to diffusing substances than the plasma membrane. During cell division, however, the nuclear membrane disappears entirely, apparently dissolving in the general protoplasm, due to some change in either the nucleoplasm or the cytoplasm or both. At the end of cell division a new nuclear membrane is formed, in each of the two new cells, at the surface of contact between the chromosomes and the cytoplasm (Fig. 8). The nuclear membrane controls the diffusion of dissolved substances between nucleus and cytoplasm, just as the plasma membrane controls that between the cytoplasm and the external medium.

Surface membranes, or phase-boundary films, must also surround every formed body—plastids, granules, fibrils, etc.—within the cell. Not only these microscopically visible bodies but also the ultramicroscopic phases of the protoplasm must each have a surface membrane of specific composition and structure depending on the compositions of the two phases it separates. The whole cell is thus made up of a large number of microscopic and ultramicroscopic "reaction chambers" separated by surface membranes of varying permeabilities which limit the diffusion and mixture of dissolved substances. This film-pervaded structure is of great importance in the chemical processes of the living cell. Because of this complex structure, the chemical reactions in the cell occur under very different conditions than in a simple system like a beaker of water; despite its small size, the cell is a highly complex "chemical engine" in which many different reactions may occur simultaneously but more or less independently, the interactions of various substances being largely controlled by the limitation of their diffusion from one phase to another by the phase-boundary membranes.

Absorption, secretion and excretion.—The passage of dissolved substances into cells is called, in general, *absorption.* The passage of dissolved substances out of the cells is called *secretion* or *excretion.* The term excretion is usually applied to the elimination of waste products of metabolism, which are usually relatively simple substances (such as carbon dioxide, ammonia, etc.) produced by the decomposition of more complex food substances within the cell. The term secretion is usually applied to more complex substances synthesized within the cell, which usually serve some function of use to the organism after leaving the cells which produced them (Chapter XIV). The distinction between these two terms is, however, not very sharp.

Absorption, secretion, and excretion are primarily processes of diffusion. Not all of the phenomena of absorption and secretion by living cells, however, can be explained by the simple laws of diffusion and osmosis. In some cases substances pass into, out of, or through living cells in a different way from what we should expect on the basis of these laws; *e.g.*, a substance (water or a solute) may pass through the cell more readily in one direction than in the other, and thus actually go from a solution where it is less concentrated to one where it is more concentrated, contrary to the general law of diffusion (p. 76). Such phenomena do not "contradict" the laws of diffusion and osmosis, any more than the fact that a man or an engine can lift a weight "contradicts" the law of gravity: they simply show that some other force is at work. In simple diffusion and osmosis the energy involved is solely the kinetic energy of the diffusing molecules themselves (p. 75). In those special cases of absorption and secretion which do not conform to these general laws, some other form of energy must be involved. The source of this energy is the metabolic processes in the living cells. How this chemical energy is transformed into directed molecular movements is not yet entirely understood. There is considerable evidence, however, that *electrical* phenomena are involved in these processes, as in many other energy transformations of the living cell (Chapter XIV).

CHAPTER VI

CHEMICAL REACTIONS IN THE LIVING ORGANISM: CATALYSIS AND ENZYMES

EVERY living organism is the seat of incessant chemical reactions, which furnish both the energy for its activities and the materials for its growth. Life is coextensive, indeed practically synonymous, with this series of chemical reactions, which we call *metabolism;* when metabolism ceases, life ceases. The chemical reactions in the living organism are of many kinds and complexly interrelated. Most of these reactions can be brought about outside the organism, in the laboratory, with non-living materials. The reactions as they occur in living organisms, however, generally differ from the same reactions in non-living systems in two respects: *speed* and *specificity*. Chemical reactions, in general, proceed much more rapidly in the organism than they do, under otherwise similar conditions (of temperature, concentration, etc.), outside it; *e.g.*, glucose, dissolved in water, decomposes and oxidizes very slowly; in living cells it may do so with explosive speed (Chapter XIV). Also, the substances which compose and nourish organisms (carbohydrates, proteins, etc.) decompose and interact, outside the organism, in a great variety of ways, producing simultaneously many different reactions and diverse end products; in the living organism these reactions are much more specific and orderly; in any particular kind of cell, under given conditions, these substances undergo a definite series of reactions, in regular order, leading to a few specific end products. Thus, the spontaneous decomposition and oxidation of glucose produces over a hundred chemically different substances simultaneously; in the living cell, only a few of these are produced, and in a regular succession. This characteristic speed and specificity of chemical reactions in the organism is due to certain substances, produced in the living cells, which enormously accelerate particular reactions.

The nature and action of these substances will be discussed in the present chapter.

Catalysis.—If sucrose (ordinary sugar) be dissolved in pure water, no appreciable chemical change occurs in any practically realizable period of time. But if the solution be made acidic, the sucrose is hydrolyzed to glucose and fructose (p. 47), the hydrolysis proceeding more rapidly the more acidic the solution, *i.e.*, the greater the concentration of hydrogen ions. This reaction, as we have previously seen, is between sucrose and water:

$$C_{12}H_{22}O_{11} + H_2O \rightarrow 2\ C_6H_{12}O_6$$

In this reaction, as written, the acid does not appear at all; and, in fact, there is just as much acid in the solution at the end of the reaction as at the beginning; that is, the acid is not "used up" at all in the reaction, although this would proceed much more slowly, if at all, in its absence. Acids have a similar effect on the hydrolysis of other disaccharoses, of polysaccharoses, lipins, proteins, etc.; and many other substances act in this way on various chemical reactions. Any substance which causes or accelerates a chemical change in other substances, without itself being used up in the process, is called a *catalyst;* its action is called *catalysis;* the reaction thus brought about or accelerated is said to be *catalyzed.* Probably every truly chemical reaction can be catalyzed by some substance or substances; and conversely, practically every substance can catalyze some reaction. The relation between the catalyst and the reaction catalyzed is often very specific, though not always so; *e.g.*, hydrogen and hydroxyl ions catalyze many different reactions.

An instructive analogy, which bears many points of resemblance to catalysis, is the action of a lubricant in facilitating mechanical movement. Suppose a flat-bottomed weight to be placed on an inclined board. The weight may slide down the board very slowly, or not at all, because of friction. If some lubricating oil be put on the board the weight will now slide down much more rapidly. The action of the oil may be compared to that of a catalyst. The oil obviously does not supply any energy, or "motive power," to the system: this is supplied by the weight (gravitational potential energy) of the moving body itself; in this sense, the oil does not "cause" the movement but merely facilitates it by decreasing the frictional resistance. In the same way, a catalyst supplies no energy to the reaction which it catalyzes: the "motive power," or "cause," of the reaction is the chemical affinity (chemical potential energy) of the reacting substances; the catalyst merely decreases some kind of resistance to the reaction. In both cases, the movement (reaction) may proceed either much more slowly or apparently not at all in the absence of the lubricant (catalyst). The oil, like the catalyst, is not "used up" (*i.e.*, destroyed) by the process it accelerates, but some of it may stick to the weight and thus gradually be lost if used over and over; similarly, a catalyst may gradually be lost or inactivated in some way, even though its constituents do not appear in the products of the catalyzed reaction.

This mechanical analogy, of course, throws no light on the actual mechanism of the action of a catalyst. In most, if not all, cases, the catalyst actually combines chemically with the reacting substances (or one of them) to form an *intermediate compound*, which then decomposes (or reacts with some other substance) in such a way as to liberate, among other end products, the catalyst in its original form and amount. Thus, the hydrolysis of sucrose, catalyzed by acid, may be written as two successive reactions:

$$C_{12}H_{22}O_{11} + H_2O + H^+ \rightarrow C_{12}H_{22}O_{11} \cdot H_2O \cdot H^+ \rightarrow 2\,C_6H_{12}O_6 + H^+$$

In fact, most chemical changes really consist of several or many successive reactions. In some cases the intermediate compounds have actually been isolated and identified; in many other cases they have not yet been.

Other factors affecting velocity of reactions.—The velocity of a chemical reaction is also affected by other factors, especially by *temperature* and by the *concentration* (number of molecules per unit volume) of the reacting substances. Most chemical reactions go much faster at higher temperatures; their speed being increased, in most cases, from 2 to 4 times by a rise of 10° C. This is much greater than the effect of temperature on most physical (*i.e.*, non-chemical) processes, such as diffusion, whose rate is seldom increased as much as 1.5 times by a rise of 10° C. The magnitude of this effect also differs considerably for different chemical reactions; the amount by which the velocity of any reaction is multiplied by a rise of 10° C is called the *temperature coefficient* of that reaction.

Other things being equal, the rate of a chemical reaction is proportional to the molecular concentration of each of the reacting substances; *i.e.*, if there are twice as many molecules present in a given volume, say one liter, twice as many will react in a given time, say one minute. If we double the concentrations of *each* of two substances reacting with each other, the reaction will go four times as fast, etc. Since catalysts which form intermediate compounds are actually "reacting substances," the same rule applies to them: other things being equal, the rate of the reaction is proportional to the concentration of the catalyst; *i.e.*, with twice as much catalyst in a given volume, the reaction will go twice as fast.

Reversibility of reactions.—Every chemical reaction is, under some conditions, *reversible*, *i.e.*, can proceed in either direction. If two substances *A* and *B* combine to form a substance *C*, then *C* can also decompose into *A* and *B*. We have already seen a number of examples of reversible reactions in Chapter III; *e.g.*, the synthesis and hydrolysis of disaccharoses, polysaccharoses, proteins, etc.

The direction in which a chemical change actually proceeds under any particular conditions is determined by all factors which affect differentially the velocities of the two opposite reactions. Thus, in the system

$$A + B \underset{(2)}{\overset{(1)}{\rightleftarrows}} C$$

any factor which speeds up reaction (1) more than it does reaction (2) must result in converting more of *A* and *B* into *C;* while, conversely, any factor speeding up reaction (2) more than it does (1) must favor the decomposition of more of *C* into *A* and *B*. One of the most important of such factors is the relative *concentrations* of the reacting substances. If we increase the concentration of *A* or *B* or both, the velocity of reaction (1) is increased, and more of these substances will be converted into *C*. If, on the other hand, we increase the concentration of *C*, reaction (2) will be speeded up, and more of *C* will be decomposed into *A* and

B. Temperature will also affect the direction of change if the two opposite reactions have different temperature coefficients, as is often the case. Thus if the velocity of reaction (1) is doubled by a rise of 10° C and that of reaction (2) is trebled, raising the temperature must increase the decomposition of *C*, while lowering the temperature will increase its synthesis.

A *catalyst*, however, does *not* affect the *direction* of a chemical change. To return to our analogy of the weight on the board, it is obvious that the oil does not determine the *direction* of movement of the weight; it will facilitate its sliding up the board as well as down. The direction of movement is determined by other factors: of its "own accord" the weight will always slide down, *i.e.*, in the direction which decreases its potential energy; to make it move up, energy must be supplied from some other source. The oil, since it neither supplies nor removes energy, can not affect the direction, but only the velocity, of movement. The same principle applies to catalysis: a catalyst neither supplies nor removes *energy*, and therefore can not affect the direction, but only the velocity, of a chemical change; it must, therefore, accelerate the reaction equally in either direction. It is important to bear in mind this characteristic of catalysis: the same catalyst which catalyzes the hydrolysis of a substance (*e.g.*, sucrose, starch, or protein) will, under other conditions (of concentration, temperature, etc.), catalyze its synthesis. Under a particular set of conditions, a reaction may be, and often is, practically irreversible, *i.e.*, it proceeds practically only in one direction; but this is not the fault of the catalyst.

Enzymes.—Starch, like sucrose, can be hydrolyzed by acid; but to hydrolyze any considerable concentration of starch in a short time (*e.g.*, a 1% solution of starch in a few minutes) requires quite strong acidity and a high temperature. If this same quantity of starch, however, be mixed with a small amount of *saliva*, in neutral solution, it will be hydrolyzed very quickly, at ordinary (room or body) temperatures. A very small amount of saliva will hydrolyze a practically unlimited quantity of starch; *i.e.*, the same portion of saliva can be used over and over without losing its hydrolyzing power. From this we must conclude that the saliva contains some *catalyst* which catalyzes the hydrolysis of starch. The action of this catalyst differs from that of the acid in several respects: it produces the same effect in much smaller concentration and at a much lower temperature; its action is actually decreased by temperatures above about 40° C, and destroyed entirely at about 60° C, while that of the acid increases continuously with rising temperature; it is much more specific in its action, catalyzing the hydrolysis of starch only and of no other substance, while acid catalyzes the hydrolysis of many substances and also many other kinds of reactions. This catalyst in the saliva (called *ptyalin*) is typical of a great many catalysts found in living cells and in fluids secreted by the cells. These catalysts produced by living organisms are called *enzymes.* Enzymes, in general, are very powerful catalysts; they produce great effects in very small concentrations and at relatively low temperatures. Most enzymes produce their maximum effect at about 40° C (in some cases higher) and are destroyed at about 60° or 70° C. They are all more or less *specific* in their catalytic action; *i.e.*, each enzyme catalyzes only one kind of reaction, and, in many cases, acts on only one particular substance or a group of closely related substances. There are innumerable different enzymes produced by different kinds of organisms and cells—many different ones, in fact, in each cell—and these enzymes determine the course and rate of all the chemical reactions in the living organism.

Nature of enzymes.—Enzymes are detected and identified by their characteristic catalytic actions. No enzyme has ever been isolated as a chemically pure substance: when we attempt to isolate and purify them, the catalytic activity by which they are recognized is destroyed. The reason for this is probably that enzymes are actually not single chemical compounds, but *mixtures; i.e.*, the enzyme action depends on the simultaneous presence of two or more substances, none of which alone has any such action; when these components are separated, the "enzyme," as such, ceases to exist.

Enzymes do not diffuse through a dialyzing membrane; showing that one component, at least, is colloidal (p. 63). But, in many cases, when the colloidal and crystalloidal components of the enzyme preparation have been separated in this way, neither fraction has any enzyme action; this reappears, however, when the two are mixed again. The crystalloidal components have been identified, in some cases, as inorganic substances (*e.g.*, phosphates, iron compounds, etc.); in other cases they are relatively simple organic compounds (*e.g.*, bile salts, amino-acids, etc.). The colloidal component, or one of them, is usually or always a protein. Most enzymes are destroyed by heat, at about 60°–70° C, the same temperatures which coagulate many proteins; these two processes are very similar in other respects also. In many cases the colloidal fraction of the enzyme is destroyed by heat, while the crystalloidal fraction is not. Most enzymes are precipitated from solution by alcohol of 70% or greater concentration; so are most proteins. Here again, it is often only one part of the enzyme that is precipitated; it may be necessary to mix this precipitate with some of the remaining solution to restore the enzyme action.

The production of enzymes is part of the synthetic metabolism of the cell and depends, directly or indirectly, on the nucleus (p. 23); but after their production the enzymes may work in the cytoplasm or even outside the cell.

Mode of action of enzymes.—The catalytic action of enzymes probably always, like that of most other catalysts, involves the formation of *intermediate compounds* with the *substrate* (the substance acted on by the enzyme). These unstable enzyme-substrate compounds have, in some cases, been actually isolated and identified. Many enzyme actions, as already noted, require the presence of two or more substances, one of which is often an inorganic ion. In particular, hydrogen and hydroxyl ions play an important part in many enzyme actions. Each enzyme has its maximum effect at a certain definite degree of acidity or basicity: thus, *pepsin* is most active in a rather strongly acid solution (about 0.2% HCl); *sucrase* in a very slightly acid solution (about 0.0002% HCl); *ptyalin* in an approximately neutral solution; *trypsin* in a slightly basic solution; etc. Each enzyme has also a certain optimum temperature for its catalytic action: in most cases this is around 40° C, but in a few cases much higher (*e.g.*, for *urease* about 60° C). Below this optimum temperature, the speed of the reaction catalyzed by the enzyme increases with rising temperature, as in other chemical reactions; but above this it decreases rapidly with further rise of temperature and ceases entirely at, in most cases, about 60°–70° C. The reason for this is that the rate of the heat destruction of the enzyme increases more rapidly with rising temperature than the rate of the reaction catalyzed; so that, above the optimum temperature, the former factor outweighs the latter, while at 60°–70° the heat destruction of the enzyme is so rapid that it has no time to catalyze the other reaction to any appreciable extent.

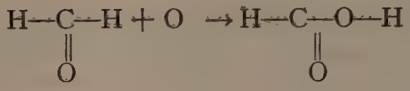
As in catalyzed reactions in general, the velocity of a reaction catalyzed by an enzyme is proportional to the concentration of the enzyme, provided the comparison be made under proper conditions. Enzymes, like catalysts in general, do not affect the direction of a reversible chemical change; the same enzyme catalyzes both the opposite reactions, *e.g.*, hydrolysis and synthesis. But under conditions in which a reaction is practically irreversible—as is the case with some metabolic reactions under the conditions in the living cell—the presence and concentration of a particular enzyme may determine the end result as well as the velocity of reaction. Thus, if a substance (*e.g.*, glucose) can react in several different ways, but *one* of these reactions is greatly accelerated by a particular enzyme, then in the presence of this enzyme the substance will be used up continuously in this particular reaction and very little of it will react in the other possible ways. Also, if several of these possible reactions are catalyzed by different enzymes, then the relative concentrations of these different enzymes will determine what proportion of the substance will react in each of these several ways. In the living cell, where there are many substances which can react with each other in many ways, the kinds and relative concentrations of enzymes present will thus determine which of the many possible reactions will occur predominantly. Thus the characteristic *specificity*, as well as *speed*, of reactions in living cells is due to the catalytic action of enzymes.

Kinds of chemical reactions in the organism.—The metabolic processes of organisms include nearly every kind of reaction known to chemistry. Most of these processes involve, at some stage, either *hydrolysis* or its reverse (the addition or removal of water) or *oxidation* or its reverse (the addition or removal of oxygen). Hydrolysis and oxidation usually result in the breaking down of more complex compounds into simpler ones (larger into smaller molecules) and also the liberation of energy (decrease of chemical potential energy); these may be called "downhill" processes, from the analogy of a weight moving down hill with decrease of potential energy. The reverse reactions (*dehydrolytic synthesis* and *reduction*), on the other hand, usually result in the building up of more complex compounds with more potential energy; these we may call "uphill" processes. Uphill processes, in general, can not take place of their "own accord," but only when energy is supplied by some simultaneous downhill process or from some extraneous source.

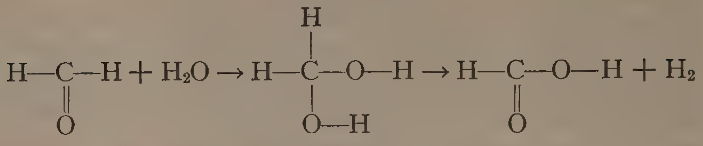
Hydrolysis is the breaking down of more complex compounds into simpler ones by chemical combination with water (p. 46). Typical hydrolytic reactions in the organism are the breaking down of di- and polysaccharoses into monosaccharoses (p. 47), of lipins into fatty acids, glycerol, etc. (p. 49), of proteins into amino-acids (p. 52), etc. This kind of reaction is involved in all *digestive* processes—which, in many organisms, occur outside the cells—and also in many metabolic processes within the cells.

Dehydrolytic synthesis (or *dehydration* synthesis) is the reverse of hydrolysis: the process by which complex carbohydrates, lipins, and proteins are built up from simpler substances (monosaccharoses, amino-acids, etc.), with the elimination of water (p. 46). These syntheses occur only within the living cell, and it is difficult to bring them about artificially. The conditions under which they occur in the cells are not yet well understood. In many cases they occur within plastids (p. 25), possibly also in other special formed bodies.

Oxidation means, literally, the combination of a compound, or some of its constituents, with *oxygen*. The same end result, however, may be reached indirectly, by a series of reactions; for instance, formaldehyde (HCHO) might be oxidized to formic acid (HCOOH) in either of the two following ways:

(1) 

$$H{-}\underset{\underset{\displaystyle O}{\|}}{C}{-}H + O \rightarrow H{-}\underset{\underset{\displaystyle O}{\|}}{C}{-}O{-}H$$

(2) 

$$H{-}\underset{\underset{\displaystyle O}{\|}}{C}{-}H + H_2O \rightarrow H{-}\overset{\overset{\displaystyle H}{|}}{\underset{\underset{\displaystyle O{-}H}{|}}{C}}{-}O{-}H \rightarrow H{-}\underset{\underset{\displaystyle O}{\|}}{C}{-}O{-}H + H_2$$

Either of these processes is called oxidation. The first, direct combination with oxygen, is called specifically *oxygenation.* The second method involves *hydration* (addition of water), followed by *dehydrogenation* (removal of hydrogen). In fact, most oxidations of organic compounds—both in the test-tube and in the living cell—actually occur in the second, indirect way; the hydrogen thus liberated is oxidized eventually to water, so that the end result is exactly the same as though the organic compound had been oxygenated directly as in reaction (1) above. Biological oxidations may, then, be said to involve *either* the addition of oxygen to, or the removal of hydrogen from, organic compounds. Since carbon and hydrogen, the chief constituents of organic compounds, both have strong chemical affinity for oxygen, these oxidations liberate a great deal of energy. The greatest part of the energy expended by most organisms is derived from the oxidation of organic food substances within the cells. The oxidation of such substances—carbohydrates, fats, etc.—involves a whole series of reactions (p. 113), in the course of which these compounds are broken down to much simpler ones and their carbon and hydrogen oxidized finally to *carbon dioxide* and *water.*

Reduction is the reverse of oxidation: the removal of oxygen (*deoxygenation*) or addition of hydrogen (*hydrogenation*). Some of the oxidative reactions of organisms are actually reversible under certain conditions in the cells, but some others are irreversible: most organisms, except green plants, are incapable of reducing carbon dioxide, so that their oxidation processes are, in this respect, irreversible.

There are other reactions in the cell which do not seem, as judged by their end results, to involve the addition or removal of water or its elements. Many of these, however, are actually series of successive reactions often involving alternate hydration and dehydration, or oxidation and reduction, as intermediate stages. Some of these reactions are decompositions, resulting in the *fragmentation* of more complex molecules into simpler ones; others are the reverse of these, syntheses involving the *condensation* of simpler molecules into more complex ones. Besides decompositions and syntheses, there are other reactions resulting only in internal rearrangements of atoms or radicals within the molecule; these changes may be effected by alternate hydration and dehydration, or by simultaneous oxidation and reduction at different points of the same molecule (p. 113).

All these reactions in the living cell are intimately related to and bound up with each other. The end products of one reaction furnish the materials for the next one; the reduction of one substance is effected by the simultaneous oxidation of another; "uphill" reactions are effected by the absorption of energy liberated by simultaneous "downhill" reactions; etc. In particular, *water* is involved, in one way or another, in most or perhaps all of these reactions. This whole complex of chemical reactions within the living cell constitutes *metabolism.*

Kinds of enzymes.—All these different reactions are catalyzed in the organism by different, more or less specific, enzymes. The various kinds of enzymes are classified and named according to the reactions they catalyze: first according to the *kind* of reaction catalyzed, then according to the particular substance or group of substances acted on. The name of each enzyme, or group of enzymes, is formed by adding the suffix *ase* to the name of its substrate (there are also a number of older names ending in *in* not formed in this way). Since most of the reactions in the organism involve hydrolysis or oxidation, or the reverse reactions, the two chief groups of enzymes are the *hydrolyzing enzymes* (or *hydrolases*) and the *oxidizing enzymes* (or *oxidases*); the former catalyze hydrolyses and dehydrolytic syntheses; the latter catalyze oxidations and reductions. The other kinds of reactions mentioned above (fragmentations, etc.) are also catalyzed by specific enzymes which are, in general, not included in either of these two main classes.

Enzymes are also classified as *extracellular enzymes* and *intracellular enzymes:* the former do their work outside the cells by which they are produced (*e.g.*, in the cavity of the digestive system, or entirely outside the organism); the latter normally work only inside the cells. Many of the typical hydrolyzing enzymes (*digestive* enzymes) are extracellular enzymes; but these same enzymes may also work in the same way inside the cells. Most other enzymes (oxidases, etc.) are strictly intracellular in the living organism; they can be extracted from the cells artificially, and will then work in the same way outside them, but this extraction involves killing the cells.

Hydrolyzing enzymes.—The typical hydrolyzing enzymes, or digestive enzymes, are those which catalyze the hydrolysis of carbohydrates, lipins, and proteins. Many of these work extracellularly in the higher animals (in the cavity of the digestive system), and in some lower organisms (fungi, bacteria, etc.) where they work outside the organism in the surrounding fluids; but the same or very similar enzymes also work intracellularly in the cells of these, as well as other, organisms. Outside the cells, these reactions go practically completely in the direction of hydrolysis, but inside the cells the same enyzmes presumably catalyze the reverse, synthetic, reactions under proper conditions.

Some of the important hydrolyzing enzymes, found in many kinds of organisms, are the following:

Enzymes	*Substances hydrolyzed*	*Products of hydrolysis*
Saccharases (or carbohydrases)	Carbohydrates	
amylase	starch	maltose
maltase	maltose	glucose
sucrase	sucrose	glucose and fructose
lactase	lactose	glucose and galactose
Lipases (or esterases)	Lipins (and other esters)	fatty acids, glycerol, etc.
Proteases	Proteins	
pepsin	proteins (in acid medium)	proteoses and peptones
trypsin	proteins (in basic medium)	amino-acids
erepsin	proteoses and peptones	amino-acids

Oxidizing enzymes.—All living cells contain oxidizing enzymes, which catalyze oxidative processes within the cells. Many of these oxidative processes are complex series of successive reactions, involving hydration, dehydrogenation, oxidation of hydrogen, etc. The oxidizing enzymes therefore comprise many kinds of catalysts, catalyzing these various kinds of reactions.

Many oxidizing enzymes contain the element *iron*. This element has the capacity of alternate oxidation and reduction; *e.g.*,

$$2\ FeO + O \xrightarrow{\text{oxidation}} Fe_2O_3 \xrightarrow{\text{reduction}} 2\ FeO + O$$

In this way, it is able to combine with oxygen and "transfer" it to some other substance, whose oxidation is thereby catalyzed. The oxidizing enzymes in the cells contain iron as a constituent of complex organic compounds, different ones of which act specifically on different classes of food substances. The most important of these iron-containing oxidases are hematin-protein compounds, related to hemoglobin (p. 54), called *cytochromes*, found in all cells.

Another important type of catalysts concerned in oxidation processes are *hydrogen acceptors*, substances capable of alternate hydrogenation and dehydrogenation. The most important substance of this type is *glutathione*, a simple peptide, found in many or perhaps all cells. It works in this way:

$$\begin{array}{ll}
\text{oxidized glutathione} & C_8H_{13}O_5N_2S - SN_2O_5H_{13}C_8 \\
\text{reduction (hydrogenation)} & \qquad\qquad + H_2 \\
 & \qquad\qquad \downarrow \\
\text{reduced glutathione} & C_8H_{13}O_5N_2SH + HSN_2O_5H_{13}C_8 \\
\text{oxidation (dehydrogenation)} & \qquad\qquad + O_2 \\
 & \qquad\qquad \downarrow \\
 & C_8H_{13}O_5N_2S - SN_2O_5H_{13}C_8 + H_2O_2
\end{array}$$

In this way, it is able to "accept" hydrogen from other substances, thus oxidizing (dehydrogenating) them, and "transfer" this hydrogen to the oxygen. The oxidation (dehydrogenation) of glutathione is itself catalyzed by iron-containing oxidases. The hydrogen peroxide (H_2O_2) formed as a by-product of this reaction is poisonous to protoplasm if allowed to accumulate in any considerable concentration; it is, however, ordinarily decomposed

$$H_2O_2 \longrightarrow H_2O + O$$

as fast as it is produced, this reaction being catalyzed by another iron-containing enzyme, called *catalase*, found in almost all cells.

These oxidizing enzymes also catalyze the reverse reactions, reductions, in so far as these are possible under the conditions in the cells.

Other enzymes catalyze various reactions in the cell which cannot be classified exactly as hydrolytic or oxidative. A few of the most important of these, found in many or all cells, are the following:

Glycolytic enzymes (or *glycases*) catalyze the fragmentation of glucose (or other monosaccharoses) into simpler organic substances, such as lactic acid ($C_3H_6O_3$); these reactions are reversible in the cells.

Aminases catalyze *deamination*, the removal of amino (NH_2) radicals from amino-acids, organic bases, etc., and also the reverse process, *amination*, by which these substances are synthesized from ammonia and organic compounds.

Carboxylases catalyze *decarboxylation*, the splitting off of CO_2 from organic acids; this reaction is apparently completely irreversible in all cells.

We shall have frequent occasion in subsequent chapters to refer to all these and various other enzymes in connection with the reactions which they catalyze, since these metabolic reactions are the essential basis of all the activities of living organisms.

CHAPTER VII

NUTRITION OF THE ANIMAL CELL

Of all the activities of a living organism, the most essential to its life are those involved in securing food and the changes which the food substances undergo within the organism. For it is solely from their food that organisms derive both the energy for their activities and the matter for their growth and reproduction. No organism can long continue its activities—*i.e.*, continue to be alive—without food. And even for the limited time it can do so, this is only by virtue of the food previously stored up in its body or by consuming part of its own protoplasm, which had previously been built up from food substances. All the activities which constitute life are thus, directly or indirectly, dependent on food.

Food may be defined as any substance which can either (1) yield *energy* for the activities of an organism, or (2) supply *matter* for the formation of protoplasm or of any material necessary to the structure or activities of the organism (*e.g.*, skeletal materials, body-fluids, enzymes, etc.).

All the processes involved in securing food materials, their transformations (chemical changes) within the organism, and the elimination of their waste products, are included in the general term *nutrition*. This includes the *essential nutritive processes* (metabolism) taking place in every cell, and various *accessory nutritive processes* by which food materials are taken into the organism and distributed to all its parts and the waste products of metabolism eliminated. These accessory nutritive processes and the mechanisms by which they are effected differ widely in different kinds of organisms. In this and the following chapters we shall study the nutritive processes in various types of organisms; beginning with unicellular forms, in which all these processes take place in a single cell, and proceeding to the more complex, multicellular plants and animals, in which the various accessory nutritive processes are performed by different groups of cells (organs), each specialized for the performance of some one process. We shall consider first the nutrition of the animal cell, because this is essentially simpler than that of the plant cell.

Animal nutrition.—The primary characteristic of *animal* nutrition, as distinguished from that of plants, is the inability of animal cells to synthesize organic compounds from inorganic substances; the food materials which the animal takes in from outside must therefore contain organic compounds (carbohydrates, proteins, etc.). These food substances can only be obtained from other organisms or their products or remains; the animal is therefore dependent on other organisms—in the final analysis, on plants—for its food. These food materials exist, for the most part, in solid form. The *ingestion* of solid food is therefore characteristic of most animals; this mode of nutrition is called *holozoic*.

The principal food substances of animals, their uses, and the sources from which animals obtain them, are summarized in the following table:

Food Substances	*Uses in the Animal*	*Sources*
Oxygen	Yields energy by oxidation of organic compounds.	Free oxygen in air and dissolved in water.
Water	Essential component of protoplasm and body-fluids.	Drunk or absorbed directly; also present in organic food materials.
Salts	Essential components of protoplasm and body-fluids.	Dissolved in water; also present in organic food materials.
Carbohydrates Fats	Chiefly yield energy by oxidation; also supply matter for synthesis of proteins, phospholipins, etc.	Other organisms
Proteins	Essential components of protoplasm; also yield energy by oxidation.	

Unicellular animals.—There are many kinds—some thousands of species—of one-celled animals (protozoa), which differ in size, form, intracellular structure, mode of locomotion, etc.; some species live in fresh water, some in salt water, some in moist soil, and some inside the bodies of other organisms. Two of the commonest fresh-water protozoa, which have long been favorite objects of study, are Amoeba (Fig. 11) and Paramecium (Fig. 27), representing, respectively, one of the simplest and one of the most complex types of unicellular animals. These organisms may be studied as examples of the typically animal (holozoic) mode of nutrition, reduced, so to speak, to its simplest terms.

Ingestion.—The food materials of protozoa are chiefly other unicellular organisms (algae, bacteria, etc.). These are ingested in various ways by different protozoa. Amoeba creeps about on submerged objects by a kind of "flowing" process: the protoplasm, at any point of its surface, may flow out as a blunt, rounded projection, called a *pseudopodium* (Fig. 26, *ps*); the rest of the amoeba then flows into this pseudopodium; thus the organism moves from place to place, in any direction. When the amoeba comes in contact with food material, pseudopodia flow out on each side of the food particle, surrounding and finally engulfing it. The food material thus comes to lie inside the amoeba, within a vacuole formed by the drop of water taken in with it, called a *food vacuole* (Fig. 26, *fv*).

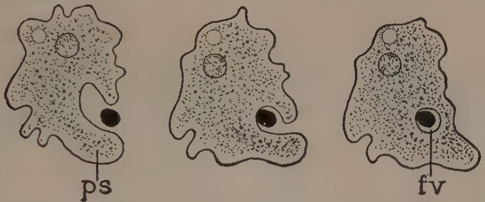


FIG. 26.—Amoeba ingesting a particle of food. *ps*, pseudopodium; *fv*, food vacuole.

Paramecium swims about in the water by means of hair-like processes, called *cilia*, with which its whole surface is covered (Fig. 27). On one side of the paramecium is a deep groove, the *oral groove*, lined with cilia. At the bottom of this groove is an opening called the *mouth*, leading into a short cylindrical cavity called the *gullet*. The gullet, at its inner end, opens directly into the cytoplasm of the cell. The swimming movement of the organism, together with the beating of the cilia in the oral groove, keeps a stream of water flowing into the mouth and gullet. The minute organisms, chiefly bacteria, carried in with this water, constitute the food of the paramecium. At the inner end of the gullet, these food materials and the water taken in with them form *food vacuoles*. There is a quite regular streaming movement (*cyclosis*) of the cytoplasm, which carries the food vacuoles around the cell in a definite path.

Digestion.—In all holozoic protozoa the ingested food material, together with the water taken in with it, forms food vacuoles. These vacuoles are bounded by surface membranes which were originally part of the plasma membrane of the cell at the point where the food was ingested. Thus the food, although inside the cell, is not yet actually in the protoplasm. Most of the organic food substances (starch, fats, proteins, etc.) contained in the ingested food materials are in insoluble or indiffusible (colloidal) form. Before they can be absorbed into the protoplasm they must be hydrolyzed into simpler substances which can diffuse through the vacuolar membrane. This hydrolytic process is called *digestion.*

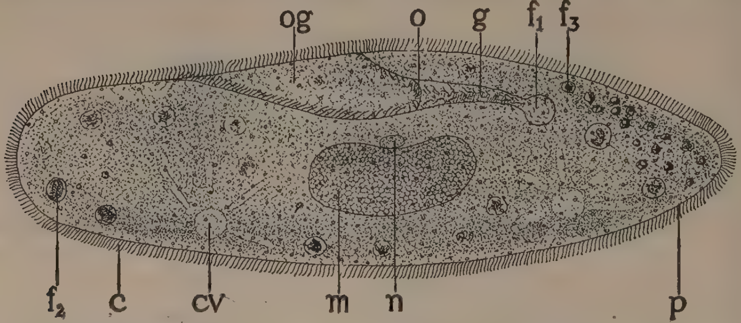


FIG. 27.—Paramecium. *n*, micronucleus or true nucleus; *m*, macronucleus; *p*, pellicle or cell membrane; *c*, cilia; *cv*, contractile vacuole; *og*, oral groove; *o*, mouth; *g*, gullet; f_1, food vacuole just formed; f_2, food vacuole during the process of digestion; f_3, food vacuole at or near the completion of digestion and absorption.

Digestion is accomplished by the catalytic action of hydrolyzing enzymes which are produced by the protoplasm of the cell and secreted into the food vacuoles. There are many different digestive enzymes, each of which is quite specific in its ability to catalyze the hydrolysis of a particular class of food substances (or, in some cases, even of a single substance). The most important digestive enzymes, with the food substances they act on, have been listed previously (p. 104). Not all protozoa produce all of these different enzymes, and not all of them, therefore, can digest and utilize as food the same substances. Some species, for instance, do not produce amylase, and therefore cannot digest starch, while others do. The ability of different species to digest other carbohydrates (*e.g.*, sucrose) also varies according to the presence or absence of the appropriate enzymes (p. 98). All species, however, produce proteases, which hydrolyze proteins to amino-acids. Fats and other lipins may be hydrolyzed by lipases, to fatty acids, glycerol, etc. (p. 50); or some lipins may be absorbed without hydrolysis, as the vacuolar membrane may be permeable to them (p. 86).

Absorption.—As the final result of the digestive processes, the contents of the food vacuoles come to consist of a solution of glucose, amino-acids, glycerol, fatty acids, etc. As the membrane surrounding the vacuole is permeable to these substances, and as they are more concentrated in the vacuole than in the surrounding protoplasm, they must, according to the laws of diffusion and osmosis, diffuse from the food vacuole into the protoplasm. There are probably other factors, physical and chemical (p. 92), involved in the absorption of these substances from the food vacuoles, but the principal one is this difference of concentration, which is maintained by the digestive processes continually producing these substances in the food vacuole, on the one hand, and the metabolic processes continually transforming them within the protoplasm, on the other hand.

Some food substances (*e.g.*, salts, monosaccharoses, and in some cases lipins) undergo no chemical changes (digestion) in the food vacuoles, but are absorbed directly. Most of the water is also absorbed from the food vacuole, because of the greater osmotic pressure of the protoplasm due to its colloidal components (proteins, etc.); so that eventually there is nothing left in the food vacuole but the indigestible solid residues (cellulose, etc.), which are finally *egested*. The process of egestion (or *defecation*) is just the reverse of ingestion: the food vacuole comes to the surface of the cell and its contents are ejected. In Amoeba egestion, like ingestion, may take place at any point of the surface; in Paramecium it occurs always at one definite point on the surface of the cell, the *anal spot.*

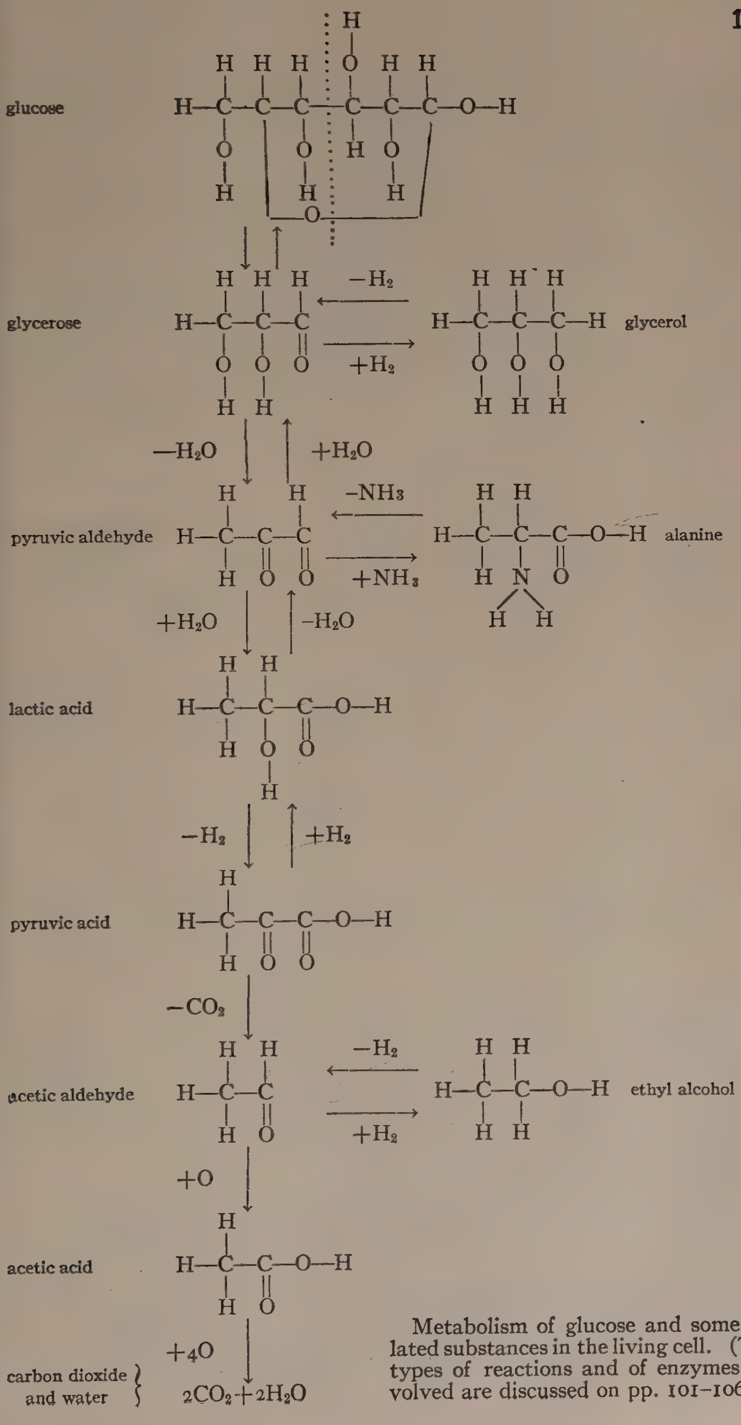
Metabolism.—Within the protoplasm, the absorbed food substances undergo various chemical changes, called collectively *metabolism*. These processes may be divided roughly into two groups: *destructive* metabolism (also called *catabolism*), by which organic food substances are *decomposed* and *oxidized*, with liberation of their potential energy (p. 13); and *constructive* metabolism (also called *anabolism*), by which some of the food substances are *synthesized* into more complex compounds to be *stored* in the cell as reserve food or *assimilated* into protoplasm.

Destructive metabolism.—In the animal cell, the greater part of the food is consumed in destructive metabolism, which supplies energy for the activities of the animal. This energy is expended in various forms (p. 14), chiefly as mechanical energy (movements) and heat. Since all forms of energy are entirely convertible into heat, but heat is not entirely convertible into other forms of energy (p. 14), it is convenient to express *quantity* of energy in units of heat. The most convenient unit of energy for our purpose is the *large Calorie*,[1] which is the quantity of heat required to raise the temperature of *one kilogram* of water *one degree centigrade*. Substances which yield energy by their oxidation in the organism are called *fuel* substances, and their *fuel value* is expressed in Calories per gram; *i.e.*, the number of Calories of energy liberated (transformed from potential to kinetic) by the oxidation of one gram of the substance in the organism.

Carbohydrates are the principal fuel substances of most organisms. Carbohydrates are absorbed, after digestion, as monosaccharoses—chiefly *glucose*, which is the principal end product of digestion of the most abundant carbohydrates (p. 47). Other monosaccharoses (fructose, etc.) after absorption may be converted into glucose within the cell. The successive steps in the destructive metabolism of glucose, so far as they are known, are shown in the diagram on page 113. This process is a complex series of reactions, involving fragmentation, hydration and dehydration, oxidation, decarboxylation, etc., each of these reactions being catalyzed by specific enzymes in the cell (p. 103). The intermediate products are spoken of as *metabolic fragments*. Many of

---

[1] This unit is spelled with an initial capital to distinguish it from the small calorie (gram calorie), a unit equal to one-thousandth of a large Calorie. The large Calorie is used throughout this book, because it is the unit generally employed in connection with nutrition.


glucose
glycerose
$-H_2$
$+H_2$
glycerol
$-H_2O$
$+H_2O$
pyruvic aldehyde
$-NH_3$
$+NH_3$
alanine
$+H_2O$
$-H_2O$
lactic acid
$-H_2$
$+H_2$
pyruvic acid
$-CO_2$
acetic aldehyde
$-H_2$
$+H_2$
ethyl alcohol
$+O$
acetic acid
$+4O$
carbon dioxide and water
$2CO_2+2H_2O$

Metabolism of glucose and some related substances in the living cell. (The types of reactions and of enzymes involved are discussed on pp. 101–106.)

these reactions are reversible in the cell, but the final ones, involving the production of carbon dioxide, are not. Not all the steps shown here need necessarily be passed through in every cell—some of them may perhaps be skipped by "short cuts"; but, on the other hand, there are probably other intermediate steps between some of those shown here, so that the whole process is undoubtedly more, rather than less, complex than indicated in our diagram. The end result of this series of reactions is the complete oxidation of the glucose to carbon dioxide and water; the whole process, disregarding the intermediate steps, may be represented by the chemical equation:

$$C_6H_{12}O_6 + 6\,O_2 \longrightarrow 6\,CO_2 + 6\,H_2O$$

In this chemical change, the potential energy of glucose and free oxygen is transformed into kinetic energy, which appears in various forms in the activities of the organism. The complete oxidation of one gram of carbohydrate liberates about *four Calories* of energy.

Fats also serve, directly or indirectly, as fuel substances. Fats are absorbed, after digestion, as *glycerol* and *fatty acids*, or are hydrolyzed to these substances after absorption. Glycerol is oxidized to *glycerose*, which is further metabolized as shown on page 113. The fatty acids may be fragmented and oxidized directly to carbon dioxide and water; or they may be converted into carbohydrate, which is then metabolized as described above. In either case, the fat is finally completely oxidized to carbon dioxide and water, liberating all its potential energy. The complete oxidation of one gram of fat liberates about *nine Calories* of energy. Fats yield more energy, per gram oxidized, than carbohydrates because the fats contain a larger proportion of carbon and hydrogen (p. 48); the chemical affinity of these elements for free oxygen is the source of the energy liberated by these oxidations (p. 102).

Proteins may also serve, in part, as fuel substances. Proteins are absorbed, after digestion, as amino-acids. The first step in destructive metabolism of amino-acids is *deamination*, by which their amino radicals are split off as *ammonia;* this is shown, for one of the simpler amino-acids (alanine), on p. 113. Other amino-acids are likewise converted by deamination into non-nitrogenous compounds similar to the fragments of carbohydrate metabolism, which are then oxidized to carbon dioxide and water, liberating their potential energy. The sulphur contained in some amino-acids (p. 53) is oxidized to *sulphate*. The animal cell is incapable, however, of oxidizing ammonia, produced by deamination of the amino-acids. This substance, moreover, is poisonous to the cell if allowed to accumulate in any considerable concentration. It does not accumulate; normally, because it is converted, as fast as it is produced, into *urea*, a non-toxic substance:

$$2\ NH_3 + CO_2 \longrightarrow CO(NH_2)_2 + H_2O$$

This reaction is catalyzed by a specific enzyme, *urease*. Urea is a waste product, and is eventually excreted from the organism. Other nitrogenous waste products (*uric acid*, etc.) are produced by the decomposition of nucleic acid (p. 54), organic bases (p. 50), etc. These organic waste substances, unlike carbon dioxide and water, still contain some potential energy, which is thus lost to the organism. Proteins, and other nitrogenous organic compounds, are therefore less "efficient" as fuel substances than carbohydrates and fats, which are *completely* oxidized in the cell and liberate all their potential energy. The complete oxidation of protein (to CO_2, H_2O, and N_2) liberates about 5.5 Calories per gram, but as metabolized in the animal cell (to CO_2, H_2O, and urea) protein yields only about *four Calories* per gram.

The mechanisms whereby the chemical energy liberated by destructive metabolism is transformed into mechanical energy, electrical energy, etc., will be discussed in later chapters (Part III).

Constructive metabolism comprises the syntheses of stored food substances, of the components of protoplasm, and of the various substances secreted by cells, such as skeletal materials, enzymes, etc.

The principal stored food substances of animal cells are *glycogen* and *fats*. Glycogen is formed from glucose, by dehydrolytic synthesis (p. 101):

$$x\ C_6H_{12}O_6 \rightleftharpoons (C_6H_{10}O_5)_x + x\ H_2O$$

This reaction is reversible in the cell; thus, when glucose is abundant in the cell this reaction proceeds in the synthetic direction and glycogen is stored; when the concentration of glucose becomes low, this stored glycogen is hydrolyzed to glucose (p. 96). As the first stages in the destructive metabolism of glucose are also reversible (p. 113), glycogen may also be synthesized from these fragments (lactic acid, etc.). We have seen, moreover, that the same fragments are produced from amino-acids and fats; thus proteins and fats can also be converted (in part) into glycogen in the cell.

Fats are formed, by dehydrolytic synthesis, from fatty acids and glycerol (p. 49); this reaction is reversible in the cell. Carbohydrates are also converted into fats, by reduction: glycerose, formed by fragmentation of glucose, is reduced to glycerol (p. 113); other carbohydrate fragments (*e.g.*, acetic aldehyde) are condensed into long chains and converted, by removal of most of their oxygen, into fatty acids (p. 49). These reductions are effected by the simultaneous oxidation of additional carbohydrate: one gram of glucose produces not more than 0.36 gram of fat, the rest of this glucose being oxidized to carbon dioxide and water. One gram of glucose contains 4 Calories of potential energy; 0.36 gram of fat contains $0.36 \times 9 = 3.24$ Calories; thus the amount of fat so produced contains somewhat less potential energy than the total amount of carbohydrate consumed in producing it. Therefore, although fat contains more potential energy per gram than carbohydrate, the production of fat from carbohydrate in the cell is, *as a whole*, a "downhill" process, resulting in a decrease of potential energy. Fats are usually the most abundant stored food substances in animal cells. Fat is the most "economical" form of food reserve, because it contains more energy per gram than any other food substance.

The chief organic components of protoplasm are *proteins* and *phospholipins* (p. 56). Proteins are formed, by dehydrolytic synthesis, from amino-acids (p. 52). Some amino-acids can be synthesized from ammonia and carbohydrate fragments (p. 113). Not all the necessary amino-acids, however, can be thus synthesized in the animal cell (at least in most animals[1]); some of them must be obtained "ready made" from the food proteins. Under natural conditions, practically all the ammonia in the animal cell is derived from the deamination of amino-acids; so that the synthesis of new amino-acids really amounts to the conversion of some amino-acids into others. We may say, then, that the proteins of the cell are derived almost entirely from the proteins of the food, hydrolyzed into amino-acids during digestion and re-synthesized into proteins in the protoplasm. Each kind of cell, however, synthesizes its own particular kind of proteins from the mixture of amino-acids absorbed or formed by conversion of some amino-acids into others. The *conjugated proteins* are formed by combination of simple proteins with other radicals (p. 54), which are either derived directly from absorbed food substances (*e.g.*, phosphate), or synthesized (*e.g.*, hematin, nucleic acid, etc.) from some of the food substances or their metabolic fragments.

Phospholipins are formed, by dehydrolytic synthesis, from glycerol, fatty acids, phosphate, and organic bases (p. 50). The phosphate may be derived from inorganic salts contained in the food materials, or from phosphoproteins (p. 54). The organic bases are probably produced from some of the amino-acids. Concerning the synthesis of *sterols* in the cell, practically nothing is yet known.

The proteins and lipins thus synthesized, together with water and inorganic salts—which are absorbed as such (p. 111)—are incorporated into the protoplasm of the cell; this constitutes *assimilation*, and leads to *growth* of the cell. Assimilation and growth will be discussed further in later chapters (Part IV).

Relations between destructive and constructive metabolism.—We have, as a matter of convenience, treated destructive and constructive metabolism separately in the preceding paragraphs. In fact, however, these two groups of processes are intimately interrelated in many ways. We have seen that some of the fragments of destructive metabolism of carbohydrates are the starting points for synthesis of fats and (to some extent) proteins. Also, fragments of destructive metabolism of fats and proteins can be synthesized into carbohydrates. In short, many of the constructive (synthetic) processes prerequire the partial destruction (fragmentation) of the absorbed food substances.

---

[1] There is evidence that some protozoa can live and grow with ammonium salts as their sole scource of nitrogen, so these animals must be able to synthesize all the amino-acids necessary for them; but this is certainly not true of most animals.

Destructive metabolism supplies not only the materials, but also the *energy*, for constructive metabolism. Most of the synthetic reactions are "uphill" processes, involving increase of potential energy; this energy is derived from the more extensive "downhill" reactions (*e.g.*, oxidations) occurring simultaneously in the same cell. Thus, as we have noted above, the reduction of carbohydrate to fat, which is in itself an "uphill" reaction, is effected by the simultaneous oxidation of additional carbohydrate in such proportions that the process, considered as a whole, is a "downhill" one, with a net decrease of potential energy. All "uphill" reactions in the animal cell are similarly linked with "downhill" reactions, with the latter preponderating. *Animal metabolism as a whole* is always a "downhill" process, resulting in *decrease of potential energy.*

Most of the synthetic reactions in the cell are reversible. When the supply of food substances is more than sufficient to balance the energy expenditure of the organism, the excess is synthesized into stored food substances and into the components of protoplasm; *i.e.*, the organism *grows.* When the food supply is inadequate to balance the energy expenditure of the organism, these synthetic reactions are reversed. Under these circumstances, the organism consumes first its stored food substances (glycogen and fats). When these are exhausted, the cell begins to decompose and oxidize the organic components of its protoplasm (proteins and phospholipins); that is, to *consume itself.* This constitutes *starvation*, and if continued leads necessarily to death. Under normal conditions (adequate food supply) the cell burns—*i.e.*, oxidizes—food substances, as an engine burns fuel; only at the last extremity of starvation does it burn itself—*i.e.*, oxidize the components of its protoplasm.

The accompanying diagram (Fig. 28) indicates roughly some of the complex interrelations among the numerous chemical reactions which constitute the metabolism of an animal cell. Any such picture, however, can give but a faint idea of the vast number and complexity of the chemical reactions in the living cell.

Respiration.—*Oxygen* is continually consumed by the oxidations in the cell (p. 113). Deprivation of oxygen results in the almost immediate cessation of the activities of the animal, and if continued leads very quickly to death. This is because the cessation of oxidation results in the accumulation in the cell of *acid* substances (lactic acid, etc.), which paralyze and eventually kill the protoplasm. As the cell has no mechanism for storing free oxygen, this gas must be continuously supplied to it from outside. Protozoa (and other aquatic organisms) obtain their oxygen from that

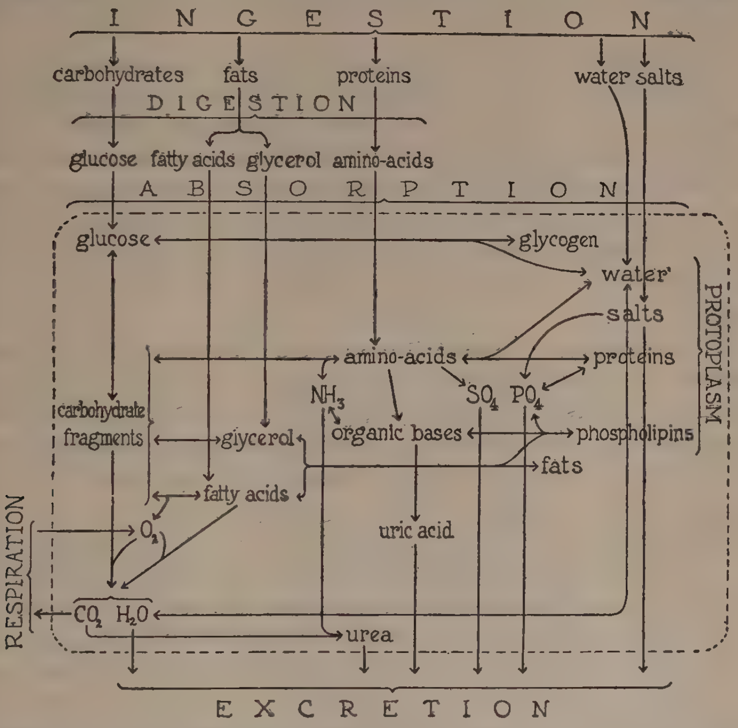

INGESTION
carbohydrates
fats
proteins
water
salts
DIGESTION
glucose
fatty acids
glycerol
amino-acids
ABSORPTION
glucose
glycogen
water
salts
amino-acids
proteins
NH_3
SO_4
PO_4
carbohydrate fragments
glycerol
organic bases
phospholipins
fats
fatty acids
O_2
uric acid
RESPIRATION
CO_2 H_2O
urea
PROTOPLASM
EXCRETION

FIG. 28.—Diagram showing the interrelations of the most important metabolic processes and the accessory nutritive processes of the animal cell. The dotted line represents the boundary of the protoplasm; the processes inside this constitute metabolism, those outside it are the accessory nutritive processes. Double-ended arrows indicate reactions which are reversible in the animal cell.

dissolved in the surrounding water. Water, in contact with air, dissolves about 0.6% of its own volume of free oxygen (at 20° C). As oxygen is being constantly used up in the cell, its concentration there is always much lower than in the surrounding water. As the cell is very permeable to this substance it must therefore, according to the laws of diffusion and osmosis, constantly diffuse from the water *into the cell.*

Carbon dioxide is continually produced by the oxidations in the cell. Accumulation of carbon dioxide also paralyzes, and may eventually kill, the animal, because it produces an acidic solution (p. 42). Its concentration in the surrounding water is normally very low, because it is consumed by the green plants in the water (p. 124) and also escapes to the air. This gas therefore, being always more concentrated in the animal cell than outside, diffuses *from the cell* to the water.

This exchange of gases (O_2 and CO_2) between the organism and its environment is called *respiration.* In unicellular animals, the mechanism of respiration is simply diffusion through the cell membranes and the protoplasm, due to the differences in concentration of these gases inside and outside the cell produced by the oxidations in the cell.

Excretion.—The decompositions and oxidations in the cell produce, also, other *waste substances:* urea, uric acid, sulphate, etc. These also escape from the cell by diffusion, their concentrations in the surrounding water being practically zero, as they are consumed by other kinds of organisms, especially bacteria (Chapter IX). The elimination of waste products of metabolism (other than CO_2) is called *excretion.* In unicellular animals, excretion is chiefly a matter of simple diffusion.

One of the chief products of oxidation in the cell is *water* (p. 113). In protozoa living in fresh water, this substance cannot escape from the cell by diffusion; on the contrary, it must diffuse *into the cell* from outside, as the osmotic pressure of the cell is greater than that of the surrounding liquid (p. 84). This would cause the cell to swell up and eventually burst; but these fresh-water protozoa have a special mechanism, the *contractile vacuole,* which continually excretes this surplus water. This vacuole alternately expands, "draining" water from the surrounding protoplasm, and forcibly contracts, ejecting this water to the exterior of the organism. In Amoeba, the contractile vacuole is a simple spherical vacuole (Fig. 11); in Paramecium, there are two contractile vacuoles, one at each end of the cell, each surrounded by a radiating group of "canals" which seem to drain into it (Fig. 27). The contractile vacuole may also aid in the excretion of other waste substances.

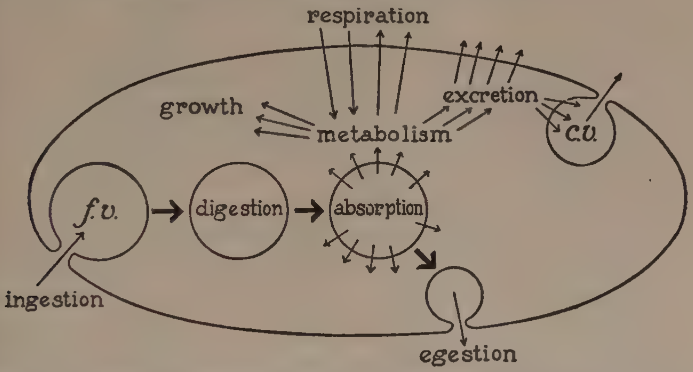


FIG. 29.—Diagram of the nutritive processes of a unicellular animal. *f.v.*, food vacuole; *c.v.*, contractile vacuole.

In protozoa living in salt water or inside the bodies of other organisms, the protoplasm is practically isotonic with the surrounding liquid (p. 84); the water produced by metabolism can therefore escape from the cell by diffusion, like other waste substances. Most of these species have no contractile vacuoles.

The accompanying diagram (Fig. 29) represents schematically the mechanisms of the accessory nutritive processes, and their relations to metabolism, in a typical holozoic protozoan.

CHAPTER VIII

NUTRITION OF THE GREEN PLANT CELL

MOST *plants* contain, in some or all of their cells, a *green* pigment, *chlorophyl*, which plays a very fundamental rôle in their nutritive processes. For this reason we speak of these organisms as "green plants," referring not primarily to their color but to their possession of chlorophyl and the mode of nutrition which this substance makes possible. The nutrition of plants *without* chlorophyl will be discussed in Chapter IX.

Nutrition of green plants.—The distinctive characteristic of green plants is their ability to synthesize organic compounds (carbohydrates, proteins, etc.) entirely from inorganic substances. The only food materials they require from outside are *carbon dioxide*, *water*, and certain inorganic *salts*. Green plants will live and grow in water containing the following salts in solution:

		Per Cent
Potassium nitrate	KNO_3	0.05
Calcium phosphate	$CaHPO_4$	0.02
Magnesium sulphate	$MgSO_4$	0.02
Iron sulphate	$FeSO_4$	trace

These salts, together with water (H_2O) and carbon dioxide (CO_2) supply all the chemical *elements* required by the plant (p. 39). Carbon dioxide is always present in the air to the extent of about 0.03% and dissolves in water in contact with air to about the same extent (at 20° C). The salts listed above are present in most natural waters. Besides these material substances, the green plant requires *light* for its nutrition. From these simple compounds, by means of the energy supplied by light, the green plant can synthesize all the substances necessary for its activities and growth. This mode of nutrition is called *holophytic*.

Unicellular green plants.—There are many species of unicellular green plants (algae), which differ from each other in size, form, and intracellular structure (Figs. 12, 30). They all differ from unicellular animals in two conspicuous characteristics: the possession of a rather thick and rigid *cell wall* (p. 27), and the presence within the cell of *chlorophyl*. The chlorophyl is usually not distributed throughout the cell, but found only in definite formed bodies called *chloroplasts* (p. 25), which differ greatly in number, size, and form in different species of algae. Some algae contain other pigments *besides* chlorophyl, so that they appear red or brown instead of green. Most algae differ from protozoa also in having no means of locomotion, but some species have one or more (usually two) whip-like processes, called *flagella*, by means of which they swim about in the water. Some algae live in fresh water, some in salt water, and some in very moist places on land; but they all live in

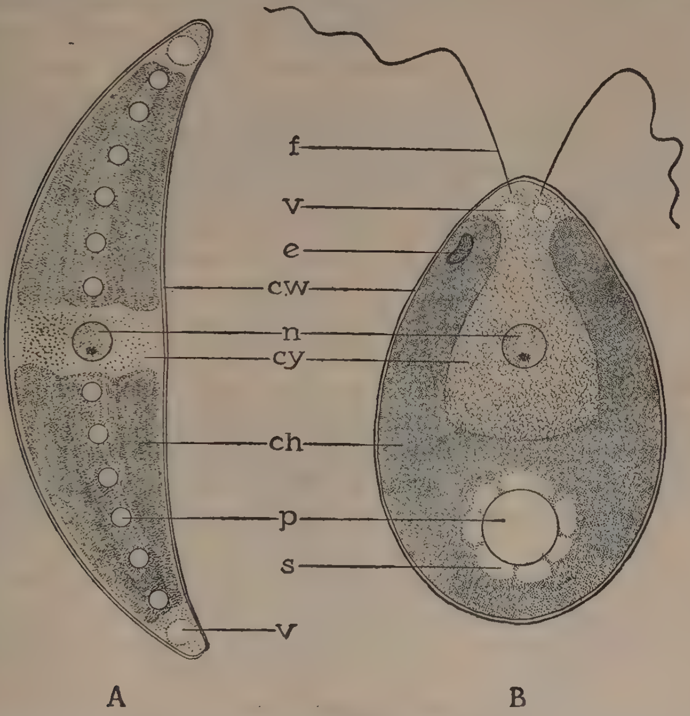


FIG. 30.—Unicellular green algae: *A*, Closterium; *B*, Chlamydomonas. *n*, nucleus; *cy*, cytoplasm; *ch*, chloroplast; *p*, pyrenoid body; *s*, starch grains; *v*, vacuole; *cw*, cell wall; *f*, flagellum; *e*, red pigment spot or "eye spot."

places more or less exposed to light, which is essential to their nutrition.

In many species of algae the cells, instead of being entirely separate, form aggregates or *colonies*, temporarily or permanently (p. 33). In these simple colonial algae the individual cells are all alike (Figs. 12, 14), and essentially independent of each other; *i.e.*, each cell can carry on all its life processes just as well if isolated from the others. Thus, though not strictly unicellular in form, they are essentially so in their nutritive processes: all the accessory nutritive functions, as well as the essential metabolic processes, are performed by each cell for itself. The unicellular and simple colonial algae therefore exemplify the green plant (holophytic) mode of nutrition in its simplest form.

Absorption.—The plant cell, being completely surrounded by a solid wall, is unable to ingest solid food materials. It has, however, no need to do so, as all the food materials it requires are present, in dissolved and diffusible form, in the surrounding water. The cell wall is quite freely permeable to all substances in crystalloidal solution (p. 87). The plasma membrane of the cell is also permeable to water and carbon dioxide and, at least slowly, to inorganic salts. These substances are used up (*i.e.*, chemically changed) by the synthetic processes within the plant cell; their concentrations are therefore usually lower inside the cell than in the surrounding water. They must, therefore, according to the laws of diffusion and osmosis, diffuse into the cell from outside. Other factors, probably electrical, are also involved in the absorption of some salts (p. 92).

Photosynthesis.—The first organic compounds synthesized by the green plant cell are *carbohydrates*, from which all the other organic substances are subsequently formed. The elementary constituents (C, H, and O) of these carbohydrates are furnished by CO_2 and H_2O. The synthesis of a simple carbohydrate, *e.g.*, glucose, from carbon dioxide and water, may be represented, as a whole, by the chemical equation:

$$6\ CO_2 + 6\ H_2O \longrightarrow C_6H_{12}O_6 + 6\ O_2$$

This process, considered as a whole, is just the reverse of the oxidation of glucose (p. 114), though the intermediate steps of these two processes as they actually occur in cells are probably very different. We have seen that the oxidation of glucose to carbon dioxide and water liberates 4 Calories of energy—*i.e.*, transforms this quantity of energy from potential to kinetic—for each gram of glucose oxidized (p. 114). Therefore the reverse process—synthesis of glucose from carbon dioxide and water—must involve the transformation of the same quantity of energy from kinetic to potential. According to the law of Conservation of Energy (p. 13), this energy must be supplied from some outside source. This source of energy is the sun, whose radiant energy, *light*, is absorbed by the chlorophyl of the plant cell. This primary organic synthesis is therefore called *photosynthesis*, *i.e.*, "synthesis by light."

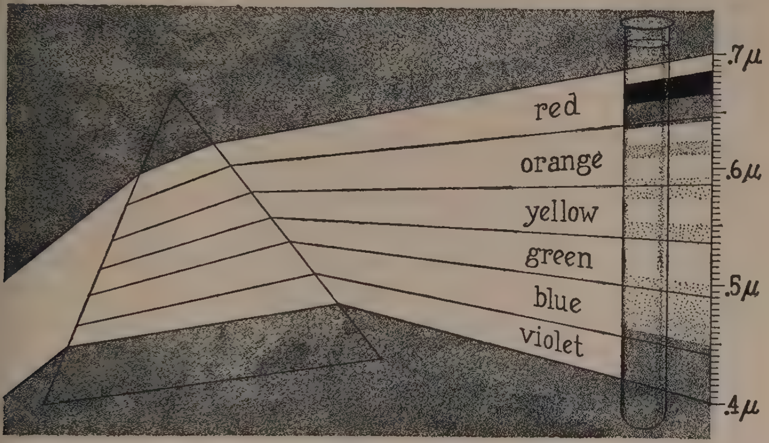


FIG. 31.—A beam of sunlight passed through a glass prism, which disperses the light, forming a spectrum, and then through a test-tube containing a solution of chlorophyl, which absorbs light in certain regions of the spectrum; the relative intensity of this absorption is indicated by the depth of shade in the absorption spectrum at the right. The scale at the right shows the wave lengths of the light in each region of the spectrum. (Adapted, in part, from Ganong.)

To understand the rôle of chlorophyl in this process, it is necessary to understand something of the absorption and the chemical activity of light. If a beam of ordinary white light (*e.g.*, sunlight) be passed through a triangular glass prism, it is broken up (*dispersed*) into a series of colors, arranged in a regular order—red, orange, yellow, green, blue, violet—called a *spectrum* (Fig. 31). Of these colors, the red consists of the longest light waves (about 7×10^{-5}

cm.) and the violet of the shortest waves (about 4×10^{-5} cm.). Beyond these two ends of the visible spectrum, there are still longer (infra-red) and shorter (ultra-violet) waves of radiant energy; but these are not visible, and are therefore not called "light." Radiant energy effects many chemical reactions, by altering the movements and positions of the electrons which bind the atoms together in molecules (p. 10). But no light waves can effect chemical action in any substance unless they are *absorbed* by that substance. The particular light waves absorbed differ for every substance, depending on the chemical composition of the substance. The *color* of any substance is that of the light waves reflected or transmitted—*i.e.*, those *not absorbed*—by it. Chlorophyl is green because it absorbs light in the red-orange and, to a lesser extent, in the blue-violet regions of the spectrum (Fig. 31). The greatest *quantity* of energy in sunlight as it reaches the surface of the earth, is in the red region of the spectrum, in just about those wave-lengths which chlorophyl absorbs to the greatest extent. The rôle of chlorophyl in photosynthesis is to absorb this radiant energy and transform it into chemical energy—ultimately into the chemical potential energy of carbohydrate and free oxygen. As would be expected from the relative absorption of different wave-lengths by chlorophyl, photosynthesis is greatest in red and least in green light.

Chlorophyl, as it exists in the plant cell, is a mixture of two compounds:

	chlorophyl *a*	$C_{55}H_{72}O_5N_4Mg$
and	chlorophyl *b*	$C_{55}H_{70}O_6N_4Mg$

These substances are complex esters, with the physical properties of lipins (soluble in alcohol, ether, etc., but not in water). They are probably largely concentrated at the surface of the chloroplast, and perhaps also at phase-boundary surfaces within the chloroplast. It is suggested, on the basis of the best evidence on the subject, that chlorophyl, under the influence of light, reacts with carbon dioxide and water in the following way:

$$\underset{\text{chlorophyl } a}{C_{55}H_{72}O_5N_4Mg} + CO_2 \rightarrow \underset{\text{chlorophyl } b}{C_{55}H_{70}O_6N_4Mg} + \underset{\text{formaldehyde}}{CH_2O}$$

$$\underset{\text{chlorophyl } b}{C_{55}H_{70}O_6N_4Mg} + H_2O \rightarrow \underset{\text{chlorophyl } a}{C_{55}H_{72}O_5N_4Mg} + O_2$$

At the end of this series of reactions the chlorophyl, it will be seen, is present in the same form and amount as at the beginning; *i.e.*, it acts as a *catalyst* (p. 94). The radiant energy absorbed by the chlorophyl is transformed, in this reaction, into the chemical potential energy of formaldehyde and free oxygen. The free oxygen is a waste product, so far as the process of photosynthesis is concerned, and escapes from the chloroplast by diffusion (p. 133). Formaldehyde is very poisonous to protoplasm, even in concentrations as low as 0.001%. It is used up, however, as fast as it is formed, by condensation to glucose (or other monosaccharoses):

$$6\ CH_2O \rightarrow C_6H_{12}O_6$$

There is relatively little energy transformation involved in this reaction, as formaldehyde and glucose contain about the same quantity of potential energy per gram.

In most plants glucose is converted, almost as fast as it is formed, into *starch*, which is deposited in the form of grains (Figs. 14, 30). This reaction is not dependent on chlorophyl or on light, as starch can be synthesized from glucose by colorless plant cells and in the dark. The *pyrenoid* bodies found in many algae (Figs. 14, 30) seem to have something to do with this process. This reaction,

$$\underset{\text{glucose}}{x\ C_6H_{12}O_6} \rightleftharpoons \underset{\text{starch}}{(C_6H_{10}O_5)_x} + x\ H_2O$$

is reversible in the plant cell, like the similar reaction, glucose ⇌ glycogen, in the animal cell (p. 115). Starch is the principal form of stored food in most plants. In some algae, glucose is converted into *fat*, which is stored as small drops (sometimes called "fat vacuoles") in the cell; the reactions involved in this synthesis are the same as in animal cells (p. 116).

The great significance of photosynthesis is this: it is the only process occurring in living organisms which is, *as a whole*, "uphill"; *i.e.*, in which potential energy is increased. The food substances from which *all* organisms derive the energy for their activities are all produced, directly or indirectly, by photosynthesis. All the energy manifested in the activities of living things can be traced back, therefore, to the radiant energy (light) of the sun, absorbed by the chlorophyl of the green plant cell and transformed into the chemical potential energy of organic compounds and free oxygen.

Synthesis of amino-acids.—From carbohydrates and inorganic salts the plant cell synthesizes all the amino-acids found in natural proteins (p. 54). These syntheses have not necessarily any direct relation to chlorophyl or to light, as they can be effected by colorless plant cells and in the dark. Indirectly, however, they are dependent on photosynthesis, for the photosynthetic products, carbohydrates, supply the most abundant elementary constituents (C, H, and O) of the amino-acids and also the *energy* for these syntheses. The other elementary constituents (N and S) are supplied by inorganic salts absorbed from the surrounding water (p. 122).

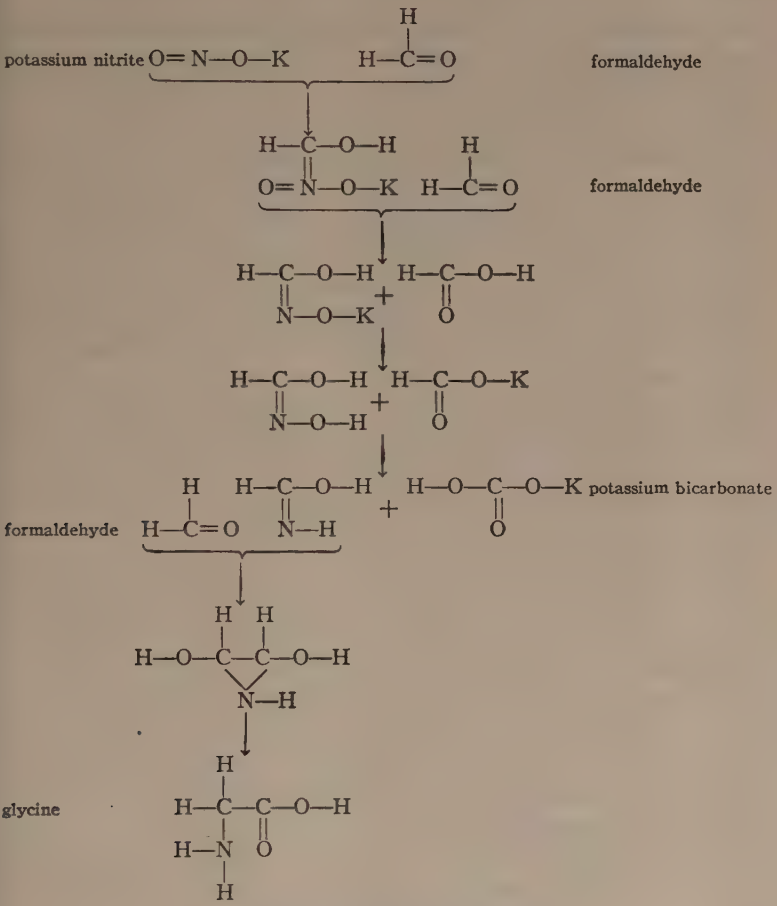
The plant cell is (like the animal cell) entirely unable to utilize free nitrogen (N_2). It can, however, utilize this element in the form of *nitrates*, *nitrites*, or *ammonium* salts (p. 42). The most abundant of these inorganic nitrogen compounds in the soil and waters are usually the nitrates. In the plant cell nitrates can be reduced to nitrites; *e.g.*,

$$\underset{\substack{\text{potassium}\\\text{nitrate}}}{KNO_3} \rightarrow \underset{\substack{\text{potassium}\\\text{nitrite}}}{KNO_2} + O$$

the oxygen liberated in this reduction being consumed by the oxidation of carbohydrate, which supplies the energy for the reaction (the reduction of nitrate to nitrite being in itself an "uphill" process, like most reductions). Nitrites react with carbohydrate fragments, derived either directly from photosynthesis or from the destructive metabolism of sugars, to form amino-acids. The synthesis of the simplest amino-acid, glycine, in the plant cell may be represented, as a whole, by the chemical equation:

$$\underset{\substack{\text{potassium}\\\text{nitrite}}}{KNO_2} + \underset{\substack{\text{carbohydrate}\\\text{fragments}}}{3\,CH_2O} \longrightarrow \underset{\text{glycine}}{CH_2NH_2COOH} + \underset{\substack{\text{potassium}\\\text{bicarbonate}}}{KHCO_3}$$

The probable intermediate steps in this process, according to the best evidence on the subject, are shown in the diagram on p. 129. Here the carbohydrate fragments are


potassium nitrite
formaldehyde
formaldehyde
potassium bicarbonate
formaldehyde
glycine

Synthesis of glycine in the plant cell

represented as formaldehyde, derived directly from photosynthesis, but other organic compounds, produced by the destructive metabolism of sugars, can act in the same way, so that this synthesis is not necessarily *directly* dependent on photosynthesis. It will be noted that part of the carbohydrate involved in this process is oxidized to an inorganic substance (carbonate); this oxidation supplies the energy for the reduction of the nitrite to NH_2 in the synthesis of the amino-acid. Other simple amino-acids are synthesized similarly; from these simple amino-acids and additional carbohydrate fragments, are synthesized the more complex amino-acids (p. 53) and other nitrogenous organic compounds (organic bases, etc.).

The plant cell can also synthesize amino-acids from ammonia and carbohydrate fragments, as we have seen that the animal cell is also able to do to some extent (p. 116). The distinctive powers of the plant cell, in regard to amino-acid synthesis, are (1) the ability to *reduce* nitrates and nitrites, and (2) the ability to synthesize the more complex amino-acids, some of which animals (at least most animals) are unable to synthesize even from other amino-acids or ammonia. These powers are possessed even by some colorless plants (Chapter IX), and are presumably due to some specific enzymes not present in animal cells. Chlorophyl has nothing to do with these processes except indirectly; *i.e.*, by producing the carbohydrate which supplies most of the matter and all of the energy for them.

The sulphur contained in some amino-acids is derived from inorganic *sulphates* (p. 122). As the sulphur in amino-acids is always in the form of SH or S-S radicals (pp. 53, 105), their synthesis involves reduction of the sulphate. This process is similar in principle to the reduction of nitrates and nitrites described above, the energy for the reduction being derived from oxidation of carbohydrate. This synthesis is also peculiar to plant cells; animals must obtain the sulphur-containing amino-acids "ready made" in their food proteins.

Other synthetic processes.—The amino-acids synthesized in the plant cell combine to form proteins just as in the animal cell (p. 116). Conjugated proteins are synthesized by combination of simple proteins with phosphates, absorbed from the surrounding water (p. 122), or with organic substances (hematin, nucleic acid, etc.) synthesized in the cell.

Fats and phospholipins are synthesized from carbohydrates, etc., just as in the animal cell (p. 116). The sterols are also synthesized from carbohydrates, directly or indirectly, but the method of this synthesis is still quite unknown. Fats, in some plants, are stored as reserve foods, as in animals; while the proteins, phospholipins, etc., are assimilated into living protoplasm. Most of these processes are essentially the same in plant and animal cells. But plant cells have, in general, greater and more varied synthetic powers than animal cells. Besides the photosynthesis of carbohydrates and the synthesis of all the amino-acids, plants also synthesize a great variety of other organic compounds which animals cannot: *cellulose* and other complex polysaccharoses, chlorophyl and other pigments, *alkaloids* (complex organic bases), various complex acids, alcohols, etc.

Destructive metabolism is essentially the same in the plant cell as in the animal cell. Under normal conditions, *glucose* is the chief fuel substance of the plant. During daylight glucose is usually produced by photosynthesis faster than it is consumed in destructive metabolism; the excess is converted into starch which is stored in the cell. During darkness photosynthesis ceases, while all the other metabolic processes continue; the concentration of glucose in the cell therefore becomes lower, and this reaction is reversed (p. 96), starch being hydrolyzed into glucose. The hydrolysis of stored food substances in plant cells is sometimes called "digestion," but it is not quite the same thing as what we ordinarily call digestion in animals, *i.e.*, the hydrolysis of ingested food substances *before* they have ever been absorbed into the protoplasm of the cell (p. 110). The hydrolysis of stored food substances within the protoplasm occurs in animal as well as plant cells, probably catalyzed by the same enzymes as those concerned in digestion in the food vacuoles (p. 111); it is purely a question of words whether we choose to call these intra-protoplasmic hydrolyses also "digestion."

The fragmentation and oxidation of glucose and of other fuel substances are probably the same in plant as in animal cells (p. 113). Since the supply of glucose, produced by photosynthesis or by hydrolysis of stored starch, is practically always adequate to balance the energy expenditure of the plant cell, other substances are seldom oxidized to liberate energy. In particular, proteins and amino-acids are not used as "energy foods" by the plant except under conditions of extreme starvation. The fats stored in some plants are re-converted to carbohydrate, at least in part, before oxidation.

The kinetic energy expended by a plant is generally much less than by an animal, as the plant does not have to move about to secure food. The plant therefore uses much less of its food substances in destructive metabolism, and has more available for constructive metabolism. Plants, in general, therefore grow faster than animals.

The accompanying diagram (Fig. 32) represents the interrelations of some of the principal processes in the metabolism of a green plant cell. Comparison of this diagram with that of Fig. 28, in the preceding chapter, will elucidate some of the chief resemblances and differences between the metabolism of a green plant cell and that of an animal cell. In general, we may say that the metabolism of the plant cell is like the metabolism of the animal cell *plus* a number of synthetic processes of which the animal is incapable.

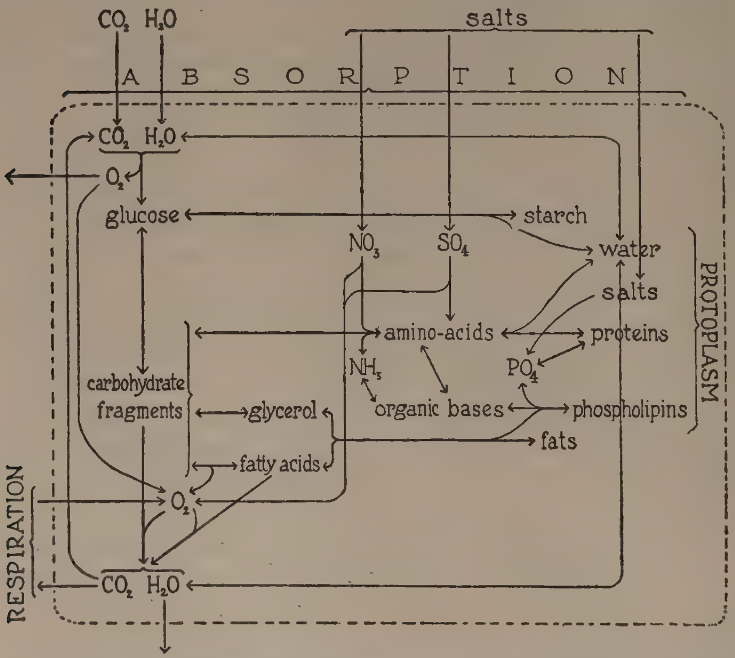

CO_2 H_2O
salts
ABSORPTION
CO_2 H_2O
O_2
glucose
starch
NO_3
SO_4
water
salts
amino-acids
proteins
NH_3
PO_4
organic bases
phospholipins
fats
carbohydrate fragments
glycerol
fatty acids
O_2
CO_2 H_2O
RESPIRATION
PROTOPLASM

FIG. 32.—Diagram showing the interrelations of the most important metabolic processes and the accessory nutritive processes of the green plant cell. The symbolism is the same as that of Fig. 28.

Respiration.—The plant cell, like the animal cell, continuously consumes O_2 and produces CO_2 in the oxidations which liberate the energy for its activities. It will be noted that this exchange of gases is exactly opposite to that involved in photosynthesis. During the daytime, photosynthesis usually exceeds oxidation. A part of the oxygen liberated by photosynthesis therefore suffices for the oxidations of the cell (the rest escaping from the cell by diffusion), while all the carbon dioxide produced by these oxidations is immediately consumed by photosynthesis. At night, however, photosynthesis ceases, but the oxidations of the cell continue. Under these circumstances, the plant cell *respires* exactly like the animal cell; *i.e.*, oxygen diffuses into the cell and carbon dioxide out of it, due to the differences in concentration of these gases inside and outside the cell, oxygen being continually consumed and carbon dioxide produced.

In the life of the plant *as a whole*, photosynthesis exceeds oxidation: the amount of organic material in the plant therefore increases; *i.e.*, the plant *grows*. Incidentally, this also decreases the amount of CO_2, and increases the amount of *free* oxygen, in the external environment (Chapter X).

Excretion.—The plant cell produces very little of any waste substances other than CO_2 and H_2O, because it ordinarily consumes only carbohydrate in its destructive metabolism. In so far as other waste substances, such as ammonia, sulphates, etc., may be produced, they are consumed again by the cell in its constructive metabolism. The plant cell, unlike the animal cell, "burns its own smoke." Some waste products, which apparently can not be used again by the plant cell, are deposited as insoluble substances in the protoplasm or vacuoles; *e.g.*, crystals of calcium oxalate are found in some plant cells.

Fresh-water algae, although living in a liquid hypotonic to their cells, can not swell up and burst, because of the rigid cell walls surrounding their cells. When the swelling of the cell, due to inward diffusion of water, reaches the limit of distensibility of the cell wall, the resistance of this wall overcomes the osmotic pressure and prevents the entrance of any more water, except as fast as it is used up in the cell (by photosynthesis). When excess water is produced in the cell by oxidation (at night), it must escape by diffusion.

The diffusion of free oxygen out of the cell, during photosynthesis, may also be regarded as a process of excretion.

The accompanying diagram (Fig. 33) represents the exchanges between a green plant cell and its environment—absorption, respiration, excretion—and their relations to the metabolic processes of the cell.

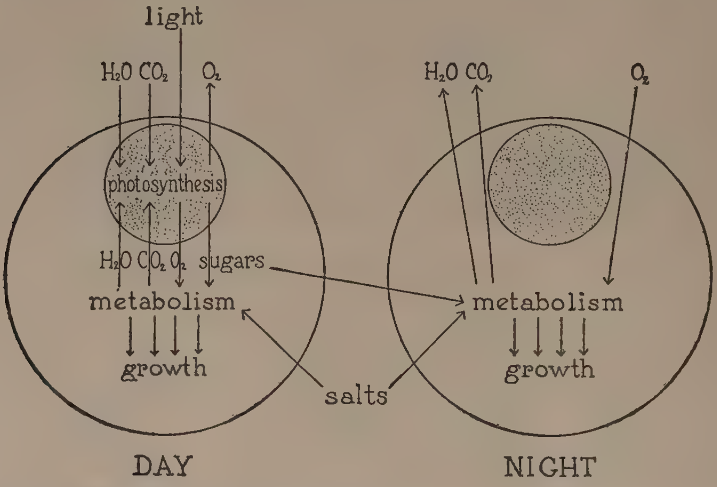


FIG. 33—Diagram of the nutritive processes of a unicellular green plant; the darker circle represents the chloroplast.

Differences between holozoic and holophytic nutrition.—

Animal	*Green plant*
Has no chlorophyl	Has chlorophyl
∴ cannot synthesize carbohydrate	∴ can synthesize carbohydrate
Can not reduce nitrates	Can reduce nitrates
Can not synthesize all amino-acids	Can synthesize all amino-acids
Dependent on other organisms for food	Independent of other organisms
Ingests solid food	Absorbs all food in solution
Moves about for food	Does not move about
∴ expends more energy	∴ expends less energy
∴ more oxidation	∴ less oxidation
∴ less constructive metabolism	∴ more constructive metabolism
Only source of energy food substances	Primary source of energy light
Nutrition *as a whole* destructive;	Nutrition *as a whole* constructive;
i.e., decreases organic compounds	*i.e.*, increases organic compounds
decreases potential energy	increases potential energy

CHAPTER IX

OTHER MODES OF NUTRITION

THE unicellular animals and plants discussed in the two preceding chapters represent the typical animal (holozoic) and the typical plant (holophytic) modes of nutrition, which are characteristic also of almost all the higher, multicellular animals and plants respectively. There are, however, among the simpler (unicellular or colonial) organisms several groups whose nutrition does not conform entirely to either of these two types. Some have modes of nutrition more or less intermediate between the two, some combine holozoic and holophytic nutrition, and others have modes of nutrition entirely different from either. In this chapter we shall consider briefly some of these "atypical" modes of nutrition.

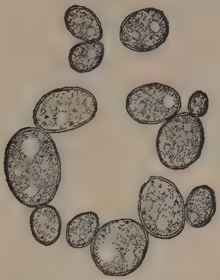


FIG. 34.—Yeast cells. The light spots are vacuoles; the nuclei are not visible in the living, unstained cells.

Fungi are a large group (about 75,000 species) of *plants without chlorophyl.* They have cellulose cell walls, are nonmotile, and cannot ingest solid food. Because of these characteristics, and because of their general resemblance to algae in structure and modes of reproduction, they are classified as plants, despite their lack of chlorophyl.

The *yeasts* (Fig. 34) are the simplest fungi, structurally; they are unicellular or form temporary, irregular aggregates, resembling some of the simplest algae except for the lack of chlorophyl. Other kinds of fungi—molds, mildews, rusts, puffballs, mushrooms, etc.—are somewhat more complex in structure, resembling some of the filamentous colonial algae. In most of them, the body consists chiefly of a long, slender, much branched thread, called a *mycelium*, which grows in or on the ground or the bodies of other organisms, living or dead. In some species the mycelium is syncytial (p. 33), in others it consists of distinct cells separated by transverse cell walls (Fig. 35). The most conspicuous parts of the larger fungi (*e.g.*, mushrooms) are the reproductive organs, which consist of complex aggregates of mycelial filaments. Any portion of the mycelium can live and grow normally if separated from the rest of the plant; so far as nutrition is concerned, all the fungi are essentially colonial rather than differentiated multicellular organisms.

We may study yeast as a simple example of the mode of nutrition of plants without chlorophyl.

Nutrition of yeast.—Yeast can not live and grow in a solution containing only inorganic substances, as a green plant can. But it will grow vigorously in a solution of the following substances:

		Per Cent
Sucrose	$C_{12}H_{22}O_{11}$	10.
Ammonium sulphate	$(NH_4)_2SO_4$	0.5
Potassium phosphate	K_2HPO_4	0.2
Calcium phosphate	$CaHPO_4$	0.02
Magnesium sulphate	$MgSO_4$	0.02
Iron sulphate	$FeSO_4$	trace

The most essential difference between this solution and the simpler one in which green plants can grow (p. 122) is the presence of an *organic* compound, sugar. The yeast, lacking chlorophyl, can not reduce carbon dioxide, and must therefore, like an animal, obtain organic substances from green plants or their products; that is, the yeast, being unable to utilize the radiant energy of sunlight by photosynthesis, must obtain its energy in the form of chemical potential energy in its food substances. The source of energy in this food solution is the sugar. The yeast can obtain its nitrogen (for synthesis of amino-acids, etc.) from inorganic compounds, though it thrives much better when the nitrogen is supplied in a *reduced* form (*e.g.*, ammonium salts) than on nitrates. From these inorganic nitrogen compounds and carbohydrate the yeast can synthesize all the amino-acids, resembling green plants in this respect. It also resembles green plants, and differs from most animals, in another respect: it can not ingest solid food, but obtains all its food substances in solution by absorption. This mode of nutrition—by *absorption* of *organic* substances in solution—is called *saprophytic.*

Yeast can utilize, as fuel substances, any of the natural monosaccharoses and various other simple organic compounds, such as glycerol, fatty acids, lactic acid and other carbohydrate fragments (p. 113). It can also utilize sucrose or maltose, which it hydrolyzes by means of the enzymes sucrase and maltase respectively (p. 104). Yeast does not, however, produce lactase or amylase, and therefore can not hydrolyze lactose or starch; these carbohydrates are therefore not available food substances for this organism.

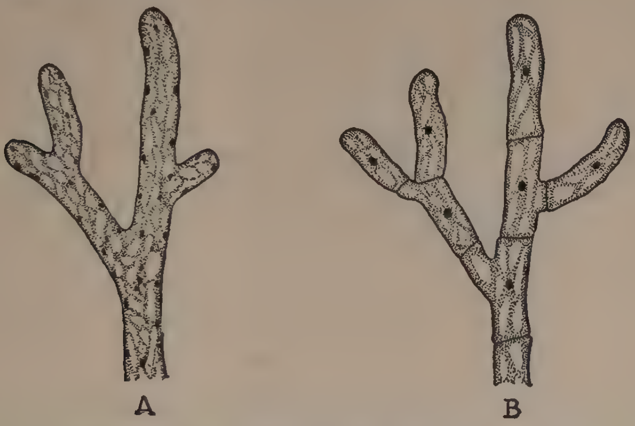


FIG. 35.—Small portions of mycelia of two common mold fungi: *A*, Mucor; *B*, Aspergillus. The black spots are nuclei.

The monosaccharoses, etc., obtained by absorption from the environment, are used by the yeast cell for destructive (energy-liberating) metabolism and for synthesis of amino-acids, etc., as in the green plant cell (p. 128). Yeast is thus intermediate in its metabolism between the animal and the green plant cell: like the animal, it is unable to synthesize carbohydrate from inorganic substances; but, like the green plant, it can synthesize all the other organic compounds it needs from carbohydrate and inorganic substances. The stored food substances of the yeast cell are *fat* and *glycogen*, as in animals. The other metabolic processes—fragmentations and oxidations, syntheses and assimilation—which are similar in animal and plant cells (p. 131), are essentially the same in the yeast cell, provided it has an adequate supply of *free oxygen*.

Anaerobic metabolism.—The yeast cell, like other cells, both animal and plant, requires a continuous supply of free oxygen for its normal metabolism; the oxygen being consumed in the oxidation of glucose or its fragments to CO_2 and H_2O, which liberates energy for the activities and for the constructive metabolism of the cell (p. 114). This kind of metabolism is called *aerobic*. But yeast can also live in the absence of free oxygen, by another kind of metabolism, called *anaerobic*. Under these circumstances glucose (or other sugars), instead of being finally oxidized to carbon dioxide and water, is decomposed into carbon dioxide and *ethyl alcohol*.

$$\text{aerobic metabolism: } C_6H_{12}O_6 + 6\ O_2 \rightarrow 6\ CO_2 + 6\ H_2O$$
$$\text{anaerobic metabolism: } C_6H_{12}O_6 \rightarrow 2\ CO_2 + 2\ C_2H_5OH$$

The intermediate steps in these two processes are similar down to a certain point, as shown in the diagram on page 113. In the absence of free oxygen, acetic aldehyde (produced by fragmentation of glucose), instead of being oxidized, is *reduced* to ethyl alcohol. This process is called *alcoholic fermentation*. The carbon dioxide and alcohol are both waste products and escape from the cell by diffusion. These products contain a little less potential energy than the amount of glucose consumed to produce them; this difference is liberated as kinetic energy, which maintains the essential life processes of the yeast cell. The amount of energy thus liberated, however, is only about 4% of that liberated by the complete oxidation of the same amount of glucose (to CO_2 and H_2O). The yeast cell, like the green plant cell, being non-motile, expends relatively little energy in its activities (p. 132). In its normal aerobic metabolism, therefore, the yeast, like the green plant, consumes but a small part of its food in destructive metabolism, and a relatively large part in constructive metabolism. In the presence of free oxygen, therefore, the yeast grows and multiplies rapidly. In anaerobic metabolism, however, since it requires about 25 times as much glucose to yield the same amount of energy, a great deal more food is consumed in destructive metabolism, and relatively little in constructive metabolism. In the absence of free oxygen, therefore, the yeast cell, though it can *live*, makes little or no *growth*. Anaerobic metabolism is thus by no means the normal or most favorable mode of nutrition for this organism.

Any plant or animal cell may produce alcohol in this way, in the absence of oxygen (p. 113). But alcohol, in any considerable concentration, is toxic to most cells; therefore they cannot survive very long under these conditions. The yeast cell has a much greater resistance to alcohol; it takes about 25% alcohol to kill this organism, but a concentration of about 15% is sufficient to stop its alcoholic fermentation, probably because some of the reactions involved are reversible (p. 96).

Nutrition of other fungi.—All fungi are nourished, like yeast, by absorbing organic substances in solution. All of them, lacking chlorophyl, must absorb carbohydrate (or other organic compounds) as a source of energy. But the various kinds of fungi differ greatly in their ability to utilize different kinds of *nitrogen* compounds. Some of them (*e.g.*, molds) can utilize *nitrates* for the synthesis of amino-acids, like green plants. But many fungi can only utilize nitrogen in a reduced form, *i.e.*, in the form of *ammonia* or similar compounds; and some must obtain their amino-acids (or some of them) "ready made," like animals. Many fungi can utilize as foods complex substances such as proteins, starch, or even cellulose. They do this by *extracellular digestion; i.e.*, by secreting enzymes (proteases, amylases, etc.) which hydrolyze these substances outside the fungus cells, which then absorb the hydrolyzed products—amino-acids, glucose, etc.

The organic compounds required by fungi can, of course, be obtained only from other organisms or their remains or products. Fungi (and other colorless plants) which obtain their food from dead organic materials are called *saprophytes;* those which feed on living organisms are called *parasites*.

Parasitism and symbiosis.—Any organism which lives on or in another living organism, from which it derives its nourishment, is called a *parasite;* the organism at whose expense the parasite lives is called its *host.* Many species of fungi, bacteria, protozoa and higher animals, and a few higher plants, are parasitic. Most parasitic animals are holozoic, *i.e.*, ingest the blood or tissues of their hosts. But all parasitic plants (and many parasitic protozoa) get their nourishment essentially like saprophytes, *i.e.*, by absorption.

Most parasites probably do little or no injury to their hosts, aside from "stealing" a certain amount of food substances from the cells or body fluids of the latter. But some of them produce definite *diseases*, either by direct injury to the cells or by producing waste products which are toxic to the host. Most diseases of animals are caused by parasitic bacteria or protozoa, while most plant diseases are due to parasitic fungi.

In some cases, the parasite is actually beneficial to its host in one way or another. In such cases, the relation of the two organisms is called *symbiosis*. Some fungi live symbiotically on or in the roots of higher plants (*e.g.*, trees); the fungus aids the host plant in absorbing water and salts from the soil, and, on the other hand, derives its organic food substances from the host. *Lichens* are fungi living symbiotically with unicellular green algae; the alga supplies the fungus with carbohydrate, while the fungus aids the alga by absorbing salts from the soil and by conserving moisture within the tangle of its mycelium. Some protozoa and higher animals have unicellular green algae living symbiotically inside their cells; the algae supply the host with carbohydrates, etc., while the animal supplies them with CO_2, water, and salts.

Flagellates are a group of simple organisms intermediate in many respects between plants and animals. Some species have chlorophyl, while others do not; most of them do not have cellulose cell walls. They are all motile, swimming by means of whip-like processes, called *flagella*. Some species are strictly unicellular, others colonial. The group as a whole grades off into the green algae on the one hand and into the typical protozoa on the other hand, and perhaps represents the common starting point of the plant and animal kingdoms (Chapter XXVI).

Some flagellates are strictly holophytic in their nutrition, some holozoic, others saprophytic or parasitic. Many flagellates, also, *combine* two or more of these modes of nutrition. *Euglena* (Fig. 36), a common freshwater flagellate, is an example of this combination of different modes of nutrition. This organism contains chlorophyl and therefore, *in the light*, can photosynthesize carbohydrate from CO_2 and H_2O; this carbohydrate is stored in the form of starch grains, just as in most green plant cells. It can also synthesize amino-acids from nitrates, like green plants. Euglena, however, can also live indefinitely *in the dark*, nourishing itself either by ingestion or by absorption of organic substances, like an animal or a saprophyte. Many other flagellates show similar versatility in their modes of nutrition.

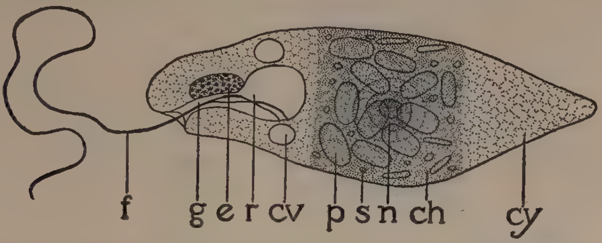


FIG. 36.—Euglena, a green flagellate. *n*, nucleus; *cy*, cytoplasm; *ch*, chloroplast; *p*, pyrenoid body; *s*, starch grain; *cv*, contractile vacuole; *r*, reservoir; *g*, gullet; *f*, flagellum; *e*, red pigment spot or "eye spot."

Bacteria (Fig. 37) are the smallest and structurally simplest, and presumably the most primitive, of all organisms (p. 29). Most bacteria have cell walls composed of cellulose or similar substances, but they have no chlorophyl. They are sometimes classified as fungi, but there is no good reason to suppose them closely related to the true fungi. They seem to be related to the Cyanophyceae (p. 30), which are holophytic plants, on the one hand, and, through certain intermediate forms, to the flagellates on the other hand (Chapter XXVI).

Within this group are found many different modes of nutrition, including some of those previously discussed and others found in no other organisms. Some bacteria, in fact, differ from all other organisms in their modes of nutrition more fundamentally than all other organisms (plants and animals) differ from each other.

Saprophytic bacteria.—Most bacteria are saprophytic, deriving their nourishment by the absorption of organic substances, in solution, from the remains or products of other organisms. These saprophytic bacteria are chiefly responsible for the *decay* of organic materials. Some species decompose or partially oxidize carbohydrates (sugars, starch, cellulose, etc.) with the production of various organic acids, alcohols, etc., while other species further oxidize these products to CO_2 and H_2O. Some of these bacteria are very specific in their food requirements, being able to utilize only one particular organic compound as a source of energy. One species decomposes the *lactose* of milk to *lactic acid;* this is responsible for the souring of milk. Another species oxidizes *ethyl alcohol*—produced by yeast—to *acetic acid*, thus producing vinegar. Some bacteria decompose proteins and amino-acids, producing various organic nitrogen compounds, some of which have very foul odors; this is called *putrefaction*. Many of these putrefactive bacteria, like most other organisms, utilize carbohydrates by preference as a source of energy, and only decompose proteins in the absence of an adequate supply of carbohydrate.

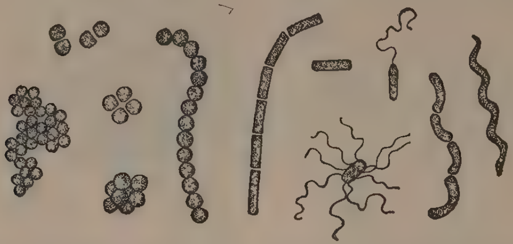


FIG. 37.—Several types of Bacteria. The spherical forms are called *cocci*, the rod-shaped forms *bacilli*, the spiral forms *spirilla*.

Some of these saprophytic bacteria are very useful in certain industries; *e.g.*, cheese-making, leather and textile manufacturing, etc. Others are harmful to man, such as those which produce *ptomaines* (poisonous organic bases) by putrefaction of proteins. In general, however, saprophytic bacteria are not only beneficial but quite essential to the continuance of life on the earth, by decomposing organic materials (dead animals and plants) which would otherwise clutter up the earth and "lock up" the essential food elements in unavailable forms (Chapter X).

Parasitic bacteria.—Many bacteria are parasitic within the bodies, or even inside the cells, of other organisms, from which they absorb soluble food substances. Most of these parasitic bacteria are practically harmless to their hosts, and some are even beneficial; *e.g.*, the cellulose bacteria which live within the intestines of certain animals, where they hydrolyze cellulose and thus make it available as food to the host. But some parasitic bacteria produce, as by-products of their metabolism, toxic substances which cause specific diseases in their hosts. These species are called *pathogenic* bacteria or "disease germs." (But not all "disease germs" are bacteria; some are protozoa or fungi.)

The filterable viruses (p. 28) are all pathogenic—indeed, it is only by their pathogenic effects that we know of their existence. These organisms are sometimes classified as bacteria. Some of these ultramicroscopic organisms, the *bacteriophages*, live parasitically within the cells of ordinary, visible bacteria (including many species pathogenic to man and other animals), and often cause the death and dissolution of these bacteria.

Anaerobic bacteria.—Most bacteria, like most other organisms, require free oxygen for their metabolism, but some kinds are anaerobic. Some species *can* live without free oxygen if necessary, like yeast; these are called *facultative anaerobes*. But there are others which *can only* live anaerobically, being killed by free oxygen; these are called *obligatory anaerobes*. The reason for this peculiarity, in such striking contrast to all other organisms, seems to be that these bacteria lack the enzyme *catalase*. This enzyme, it will be recalled, decomposes *hydrogen peroxide* (H_2O_2), which is produced in all cells by the oxidation of hydrogen (p. 105). Hydrogen peroxide, in any considerable concentration, is poisonous to protoplasm. But in almost all cells hydrogen peroxide is decomposed, as fast as it is produced, into water and oxygen, by the action of the enzyme catalase. The obligatory anaerobic bacteria apparently differ from all other organisms in not containing this enzyme. Therefore the hydrogen peroxide, produced by the oxidation of their organic food substances by free oxygen, accumulates to an extent which soon kills these bacteria. In the absence of free oxygen, they apparently obtain energy by decomposing organic substances in such a way as not to form hydrogen peroxide. Some of the most dangerous pathogenic bacteria (*e.g.*, the tetanus bacillus) are obligatory anaerobes. They may therefore be killed by means of oxidizing agents (hydrogen peroxide, iodine, etc.), or even by exposure to air.

Autotrophic bacteria.—All the bacteria so far discussed require organic compounds (*i.e.*, carbohydrates or similar substances at least) in their food, and are therefore dependent on other organisms, living or dead, for their nutrition. But there are a number of kinds of bacteria which, like green plants, require only inorganic substances for their nutrition. These bacteria obtain energy for their life processes by the *oxidation* of certain *inorganic* substances, thus differing from all other organisms. Certain species can oxidize *ammonia* (or ammonium salts) to *nitrites;* other species oxidize these nitrites further, to *nitrates* (p. 150); these are "downhill" reactions, liberating energy for the activities and constructive metabolism of these bacteria. *Sulphur bacteria* obtain energy by the oxidation of hydrogen sulphide and free sulphur to sulphates. Other kinds oxidize free hydrogen (to water), carbon monoxide (to carbon dioxide), iron salts (ferrous to ferric salts), etc. By means of the energy liberated by these oxidations, all these kinds of bacteria synthesize carbohydrate from CO_2 and H_2O, and also synthesize amino-acids, etc., like the green plant; they are thus independent of other organisms for their nutrition, and are therefore called *autotrophic*, *i.e.*, "self-nourishing."

Summary of modes of nutrition.—The various modes of nutrition among living organisms (Chapters VII, VIII, IX) may be classified as follows:

(1) *Autotrophic:* able to synthesize all the necessary organic compounds from inorganic substances, and therefore independent of other organisms for their nutrition.

  (a) *Holophytic:* obtaining energy from light by photosynthesis: green plants.

  - (b) *Autotrophic bacteria:* obtaining energy by oxidation of inorganic substances.

(2) *Heterotrophic:* unable to synthesize organic compounds entirely from inorganic substances, and therefore dependent on other organisms for their nutrition.

  - (a) *Holozoic:* obtaining organic food materials by ingestion: most animals.
  - (b) *Saprophytic* or *parasitic:* obtaining organic food substances by absorption (in many cases by the aid of extracellular digestion): fungi, most bacteria, some flagellates, some parasitic animals, a few higher plants.

(3) *Mixotrophic:* combining autotrophic and heterotrophic modes of nutrition in varying degrees: many flagellates, a few higher plants.

Of these various modes of nutrition, two—holophytic and holozoic—are almost universal among the higher, complex multicellular organisms, which therefore are sharply divisible into two very distinct groups: plants and animals (Chapters XI, XII). Among the unicellular and simple colonial organisms, however, as we have seen, these two groups merge together; there are forms on the border line between them and other forms entirely different from either of them. Figuratively speaking, we might say that protoplasm had tried, among these simpler organisms, all kinds of experiments in methods of supplying itself with matter and energy, and finally adopted only two as suitable for the maintenance of larger and more complex forms of life.

CHAPTER X

THE FOOD CYCLE

Certain chemical elements (listed on p. 39) are essential constituents of the food of all organisms. No process in living organisms transforms any *element* into another; indeed, no process of any kind occurring on our earth at the present time increases or decreases the quantity of any one of these elements. The total amount of each of these elements on the earth—in living and non-living matter together—therefore remains constant. But the chemical changes always going on in living organisms—and, to some extent, in non-living nature also—are continually changing the forms of *combination* of these elements. Not all these combinations (compounds and free elements) are useful as food substances. Each kind of organism, as we have seen, requires certain particular substances, or classes of substances, in its food. But the nutritive processes of different kinds of organisms—green plants, animals, fungi, bacteria, etc.—are complementary; *i.e.*, the food substances of one are the waste substances of another. This results in the amount of each kind of compound or free element concerned in nutrition remaining approximately constant on the earth as a whole. It is only because of this natural balance that the continuation of life on the earth is possible.

This "circulation" of the food elements in nature is called the *food cycle*. In this chapter we shall discuss briefly the cycle of each of the principal elements concerned in nutrition, and also the energy transformations involved. These relations are summarized in the accompanying diagram (Fig. 38).

Carbon is one of the most abundant constituents of organisms and their products, but is much less abundant in inorganic nature. This element constitutes 10% or more of all organisms (p. 39), but only about 0.18% of the earth as a whole. In non-living nature it occurs as free carbon (chiefly in coal), in hydrocarbons (mineral oils), limestone ($CaCO_3$ and $MgCO_3$), CO_2 and soluble carbonates in the waters, and CO_2 in the air. Most of these substances are the products of organisms. Coal is a product of decay of plants of past eras. Mineral oils may also be products of organic decay, though this is a disputed question. Limestone is, in part, a product of shell-forming animals. Carbon dioxide is chiefly produced by the respiration of organisms, though smaller amounts are also produced by fires

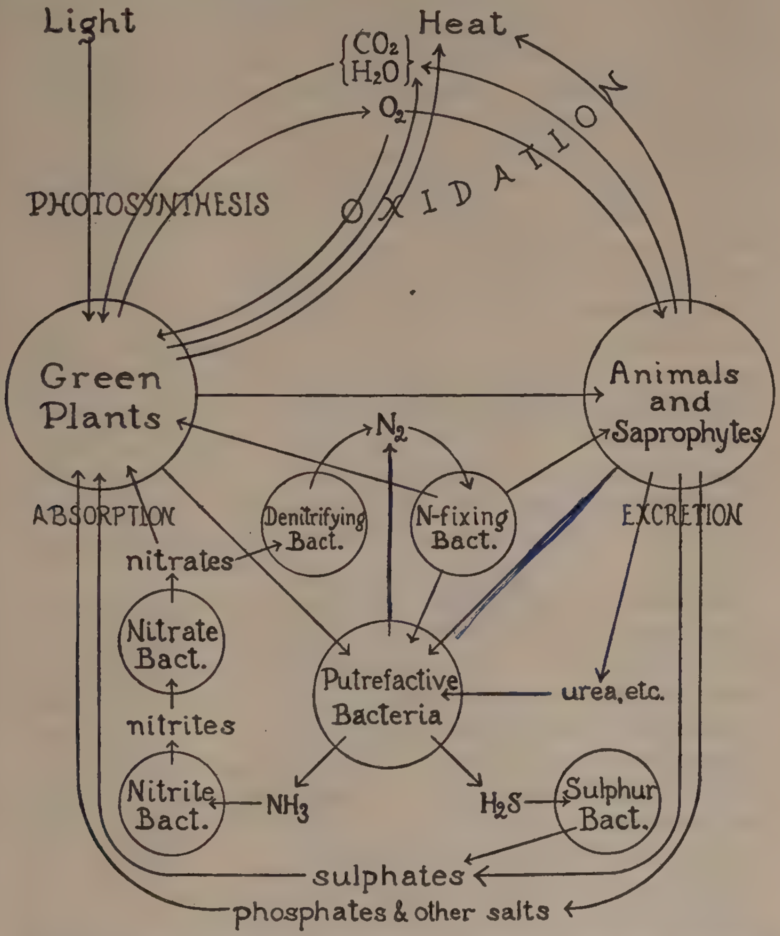

Light
Heat
CO₂
H₂O
O₂
PHOTOSYNTHESIS
OXIDATION
Green Plants
Animals and Saprophytes
N₂
Denitrifying Bact.
N-fixing Bact.
ABSORPTION
EXCRETION
nitrates
Nitrate Bact.
nitrites
Nitrite Bact.
Putrefactive Bacteria
urea, etc.
NH₃
H₂S
Sulphur Bact.
sulphates
phosphates & other salts

Fig. 38.—Diagram showing the most important nutritive interrelations of organisms, constituting the "food cycle." For explanation see text.

and by volcanoes. Almost all the carbon now existing on the earth has probably been, at some time, part of some living organism.

The chief chemical transformations of carbon in living nature are the reduction of CO_2 to organic compounds by green plants (and by autotrophic bacteria) and the oxidation of these organic compounds, by the same organisms and by others (animals, saprophytes, etc.) which get their food from these, back to CO_2. The remains of dead plants and animals are decomposed by saprophytic fungi and bacteria, and their carbon compounds finally oxidized to CO_2 also. These processes—photosynthesis on the one hand, oxidation on the other hand—result in keeping the amount of CO_2 in the air and the waters quite constant over a long period of time. The amount of CO_2 in the air at present may be less than in the remote past, because of the large amounts of carbon which have become "locked up" in coal, mineral oils, and limestone. The last is not entirely unavailable as food, however, for many plants can dissolve limestone by means of acids secreted by their roots—a kind of extracellular digestion. And the carbon of coal and oil is also now being returned to the air as CO_2 by the activities of man.

Hydrogen occurs chiefly in water, the most abundant single compound on the earth. This element is also incorporated into organic compounds by photosynthesis, and converted back to H_2O again by the oxidations of plants, animals, and bacteria. A small amount of hydrogen is liberated as free hydrogen (H_2) by anaerobic bacteria; but certain kinds of aerobic bacteria can utilize this free hydrogen as food, oxidizing it to H_2O again. Thus the hydrogen cycle is very similar to the carbon cycle.

Oxygen.—The oxygen cycle is, in a sense, exactly the opposite of the carbon and hydrogen cycles. Free oxygen (O_2) is produced as a waste product of photosynthesis. One molecule of O_2 is produced for each molecule of CO_2 consumed. The amount of free oxygen liberated in the photosynthesis of a given amount of carbohydrate is exactly equal to the amount required for the complete oxidation of this carbohydrate. In this sense, photosynthesis is the exact reverse of oxidation of carbohydrate:

$$6\ CO_2 + 6\ H_2O \underset{\text{oxidation}}{\overset{\text{photosynthesis}}{\rightleftarrows}} C_6H_{12}O_6 + 6\ O_2$$

The same thing is true, in principle, for the syntheses and oxidations of other organic compounds.

The free oxygen thus produced may be utilized by the same cell for its oxidations, or may escape from the plant by diffusion. Since the *growth* of the plant involves increase of organic compounds, green plants must, on the whole, liberate more free oxygen than they consume. But this free oxygen is consumed in the oxidations of heterotrophic organisms (animals, saprophytes, etc.), all of which get their organic compounds, directly or indirectly, from green plants. Whether oxidized in the same organism that produced it or in another, the complete oxidation of a given amount of carbohydrate (or other organic compound) must consume exactly the amount of free oxygen liberated in its original production. Since all these organic compounds are eventually oxidized to CO_2 and H_2O, the ratio between free and combined oxygen must be kept constant by these opposite life processes, photosynthesis and oxidation. The proportions of O_2 and CO_2 in the air and the waters do, in fact, remain very constant and uniform.

Nitrogen, always the fourth most abundant constituent of organisms, is, like carbon, much less abundant in inorganic nature. It constitutes about 2.5% of all organisms, but only about 0.03% of the earth as a whole. In non-living nature it occurs chiefly as free nitrogen (N_2), the chief component of *air*. In this form it is entirely unavailable as food to most organisms. But a small amount of nitrogen also occurs in combined forms, chiefly *nitrates*, in the soil and waters. Nitrates are the chief source of nitrogen for green plants (and for some fungi and bacteria). In the plant cell, the nitrates are reduced and their nitrogen incorporated into amino-acids and proteins. These plant proteins are the sole source of nitrogen for animals. The nitrogenous radicals of the amino-acids can not be oxidized by the animal cell, but are excreted in the form of simple organic compounds, chiefly *urea*. Urea is hydrolyzed by certain bacteria into *ammonia* and carbon dioxide:

$$\underset{\text{urea}}{CO(NH_2)_2} + H_2O \rightarrow 2\ NH_3 + CO_2$$

The other nitrogenous excreta of animals (uric acid, etc.) are also decomposed by bacteria, liberating ammonia. The proteins of dead plants and animals are decomposed by various putrefactive bacteria, with the liberation, in most cases, of ammonia. To some extent, these nitrogenous organic compounds are oxidized by certain kinds of bacteria which oxidize all their carbon and hydrogen, liberating *free nitrogen* (N_2).

Ammonia may serve as a source of nitrogen for green plants, but it is not the most efficient one for most of them, either because it is toxic to these plants or because it is not easily absorbed by them. Under conditions of adequate oxygen supply—*i.e.*, in well aerated soil—ammonia is rapidly oxidized by certain autotrophic bacteria, called *nitrite bacteria:*

$$NH_3 + 3\ O \rightarrow \underset{\substack{\text{nitrous}\\\text{acid}}}{HNO_2} + H_2O$$

This acid is, of course, immediately neutralized by buffer substances (p. 43); *e.g.*,

$$HNO_2 + KHCO_3 \rightarrow \underset{\substack{\text{potassium}\\\text{nitrite}}}{KNO_2} + CO_2 + H_2O$$

The nitrites, in turn, are oxidized by other species of autotrophic bacteria, called *nitrate bacteria*:

$$KNO_2 + O \rightarrow \underset{\substack{\text{potassium}\\\text{nitrate}}}{KNO_3}$$

The nitrite and nitrate bacteria are called, collectively, *nitrifying bacteria* (Fig. 39). Their activities restore to the soil those nitrogen compounds (nitrites and nitrates) most useful to green plants.

Under conditions of inadequate oxygen supply in the soil, nitrates are destroyed by certain kinds of saprophytic bacteria, called *denitrifying bacteria.* These organisms are facultative anaerobes (p. 143); in the absence of free oxygen they decompose nitrate, using its oxygen for the oxidation of carbohydrate and liberating its nitrogen as *free nitrogen*. These bacteria metabolize in this peculiar way only in the absence of free oxygen; when the oxygen supply is adequate they oxidize carbohydrate in the usual way, by means of free oxygen. They obtain their carbohydrate, like other saprophytic soil bacteria, from decaying organic matter (*humus*) in the soil. It will be seen that the condition which favors the action of the nitrifying bacteria—adequate oxygen supply—is opposed to that of the denitrifying bacteria, which reduce nitrates only in the absence of free oxygen. Since the nitrifying bacteria are autotrophic, while the denitrifiers are saprophytic, the presence of decaying organic matter in the soil is more favorable to the latter. One of the most important objects of proper cultivation of the soil is the establishment of conditions favorable to nitrification and unfavorable to denitrification.

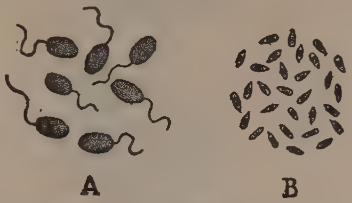


FIG. 39—Nitrifying bacteria. *A*, Nitrosomonas, a nitrite-forming bacterium; *B*, Nitrobacter, a nitrate-forming bacterium. (After Winogradsky.)

There are "leaks" at two points in the nitrogen cycle, by which nitrogen is "lost" by being liberated as free nitrogen: the action of certain oxidizing bacteria which liberate N_2 from decaying organic substances, and that of the denitrifying bacteria which liberate it from nitrates. The burning of organic materials in fires also liberates N_2. Free nitrogen is utterly useless to most organisms. But there are several kinds of bacteria which are able to *fix* (*i.e.*, chemically combine) this element to synthesize their amino-acids and proteins; these are called *nitrogen-fixing bacteria*. This fixation of nitrogen is an "uphill" process and requires the simultaneous oxidation (or decomposition) of carbohydrate to supply energy, about 100–300 grams of carbohydrate being oxidized by these bacteria for each gram of nitrogen fixed. Different species of nitrogen-fixing bacteria obtain their carbohydrate in different ways. One kind is saprophytic, obtaining carbohydrate from decaying organic matter in the soil. Another kind is symbiotic with certain green algae in the soil, obtaining carbohydrate from the algae "in return for" nitrogen compounds. Other nitrogen-fixing bacteria live symbiotically within the roots of leguminous plants—clovers, peas, beans, etc. (Fig. 40). These bacteria absorb carbohydrates from the host plant, which obtains nitrogen compounds from them; the plant, in turn, may either be eaten by animals or die and decay in the soil. These leguminous plants thus increase the fertility of the soil—*i.e.*, its content of nitrogen compounds—and are often grown for just this purpose. The soil-dwelling nitrogen-fixers also may be eaten by animals (soil protozoa, etc.) or die and decay in the soil. Thus the nitrogen-fixing bacteria

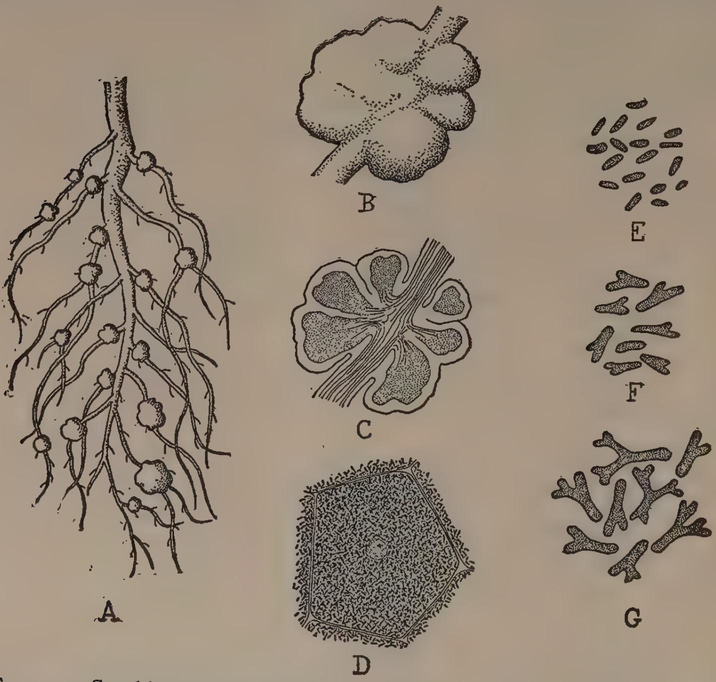


FIG. 40.—Symbiotic nitrogen-fixing bacteria. *A*, root of clover, with root nodules formed by symbiotic nitrogen-fixing bacteria (about natural size). *B*, a single nodule on root of lupin (somewhat magnified); *C*, section of same; *D*, a single cell of this nodule, filled with nitrogen-fixing bacteria. *E*, the nitrogen-fixing bacteria as they enter the root; *F*, *G*, later stages of these bacteria as they develop in the root nodules. (*B*, *C*, *D* after Woronine; *E*, *F*, *G*, after Beijerinck.)

recover nitrogen for the organic world and restore it to "circulation."

A certain amount of atmospheric nitrogen is also combined, by electrical discharges (lightning), to form ammonia, nitrates, etc., which are dissolved and washed down by the rain. In recent years, these nitrogen compounds are also being made artificially, by electrical and catalytic processes, from atmospheric nitrogen, for use as fertilizers.

Sulphur is absorbed by green plants in the form of *sulphates*, from the water or soil. In the plant cell these sulphates are reduced and their sulphur incorporated into amino-acids and proteins. In animals this protein sulphur is oxidized back to sulphates, which are excreted. From the remains of dead plants and animals some of the protein sulphur is liberated, by putrefactive bacteria, as *hydrogen sulphide* (H_2S). This substance, which is toxic to most organisms, is utilized as a source of energy by the *sulphur bacteria* (Fig. 41). These bacteria oxidize first the hydrogen of this compound, storing *free sulphur* as a reserve food substance, which they eventually oxidize to sulphate. Thus they restore the sulphur to "circulation" in a form usable by plants again.

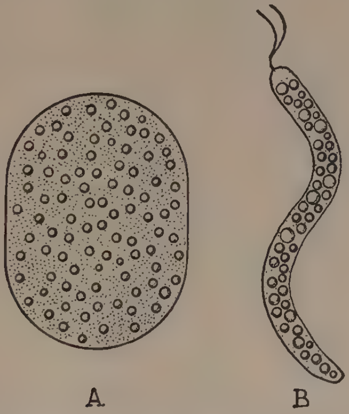


FIG. 41.—Sulphur bacteria: *A*, Achromatium (after Nadson and Wislouch); *B*, Thiospirillum (after Omeliansky). The spherical droplets are free sulphur.

Phosphorus is absorbed by plants in the form of *phosphates.* These are not reduced in the cell, but are incorporated *as phosphate radicals* into proteins, nucleic acid, phospholipins, etc. (p. 117). The decomposition of these organic compounds by animals and saprophytes liberates the phosphorus as inorganic phosphates again.

Other elements—potassium, sodium, calcium, magnesium, iron, chlorine, and others in particular organisms—are absorbed by organisms in the form of inorganic salts, and excreted again in the same form. Most of them are never incorporated into organic compounds at all, but play various essential rôles in the organism *as inorganic ions*. Some of them may enter into organic compounds—*e.g.*, iron in hematin (p. 54), magnesium in chlorophyl (p. 126), etc.—but the decomposition of these compounds by animals or saprophytes liberates these elements in their original inorganic combinations.

Energy transformations.—These chemical changes—especially the reductions and oxidations—in living organisms involve transformations of energy, which constitute life, *i.e.*, the activities of organisms. Practically all the energy manifested in these activities comes originally from the radiant energy (light) of the sun. This radiant energy is absorbed by the chlorophyl of green plants and transformed into chemical potential energy of carbohydrates (and, indirectly, other organic compounds) and free oxygen. All other organisms get their energy from these substances, taken in by ingestion or absorption and by respiration. By the metabolic processes of various organisms, these substances are all eventually converted back into those from which they were originally produced. The energy content of a given amount of any particular substance is always the same, regardless of its previous history; *e.g.*, the quantity of energy in a given amount of CO_2 and H_2O is the same whether these substances have been produced by life processes or not. It therefore follows from the law of Conservation of Energy that the energy liberated by the complete oxidation of a given amount of carbohydrate is exactly equal to that previously absorbed in the photosynthesis of this carbohydrate. But this energy is not liberated in the same *form* as that in which it was originally absorbed. Much of it is liberated directly as *heat*. Some is liberated as *mechanical energy*, *i.e.*, the movements of organisms; but this also is eventually transformed into heat (by friction, impact, etc.). Some of the energy released by oxidation of carbohydrate is transformed into chemical potential energy of other, more complex organic compounds (lipins, proteins, etc.); but these also are eventually decomposed and oxidized and their energy liberated, directly or indirectly, as heat. The same thing is true of all the other forms of energy manifested in the activities of living organisms—electrical energy, osmotic energy, surface energy, etc. (Chapter XIV)—all are eventually transformed into heat. The end result of all the activities of living nature is, therefore, the transformation of a certain amount of energy from *light* to *heat.*

The source of practically all the available light energy on our earth is the sun, where it is liberated probably by intra-atomic changes (transmutations of elements) which transform potential to kinetic energy. Only a very small fraction of this solar energy falls on our earth. Of this small fraction, the greater part falls on inanimate bodies (water, rocks, etc.), by which it is absorbed and immediately transformed into heat. Only that minute fraction of the solar energy which happens to fall on the green cells of plants and be absorbed by their chlorophyl escapes this immediate degradation. This fraction also is eventually converted entirely into heat; but by a much more roundabout series of transformations, involving all those wonderfully complex activities which constitute life.

The energy involved in life processes does not, therefore, like the matter, form a closed cycle. The matter "revolves" in a cycle, but the energy runs continually "downhill"—from light to heat—turning the wheels of life as it flows. The heat thus produced is dissipated; *i.e.*, it warms the air, water, soil, etc., and gradually becomes distributed through space. What eventually may become of this dissipated energy—whether, in any part of the universe, it may be transformed back into any "useful" form—we do not at present know. So far as our earth is concerned, all processes, in living as well as non-living things, proceed according to the Second Law of Energy: all forms of energy are continually degraded into heat and dissipated.

CHAPTER XI

NUTRITIVE MECHANISMS OF MULTICELLULAR PLANTS

We have chosen, as examples of the various modes of nutrition, unicellular or simple colonial organisms, because these exemplify in their simplest forms all the different modes of nutrition found in any organisms. The more complex multicellular organisms display no new types of metabolism or food requirements, but merely more complex "machinery" for the performance of some of the accessory nutritive processes. In unicellular and simple colonial organisms all the nutritive processes (as well as all other life processes) are performed by each cell independently. In the more complex multicellular organisms, the *essential* nutritive processes—metabolism—must still be performed by each cell for itself. But some of the *accessory* nutritive processes are performed largely or entirely by certain specialized cells or groups of cells (tissues, organs) for the whole organism. This *functional differentiation*, or "division of labor," among cells is usually accompanied by visible *structural differentiation*. Between simple colonial organisms, in which all the cells are alike, and the most complex multicellular organisms, there are many intermediate degrees of cellular differentiation and organization of the cells into tissues and organs. In this chapter we shall examine briefly the structural and functional differentiation of several plants representing successive "steps" of increasing complexity, and then, in somewhat more detail, the nutritive mechanisms of the most complex plants.

Multicellular algae.—Among the algae are found plants of various degrees of complexity, from unicellular and undifferentiated colonial forms (Chapter VIII) to multicellular plants with a considerable degree of cellular differentiation. One of the most common types of cellular differentiation among non-motile algae is the modification of certain cells as organs of *attachment.* In some filamentous algae, a single cell at one end of the filament is specialized as a *rhizoid*, or "holdfast," which attaches the filament to the soil or rocks at the bottom of the water (Fig. 42). This rhizoid cell is not only modified in shape, but also lacks chlorophyl. It is therefore dependent for its nutrition on the other cells of the filament: the sugars produced by photosynthesis in the green cells are absorbed by the rhizoid cell by osmosis through the transverse cell walls.

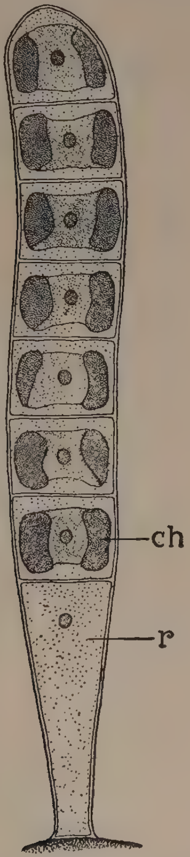


FIG. 42.—Young filament of Ulothrix, a filamentous green alga showing a slight degree of cellular differentiation. *ch*, chloroplast; *r*, rhizoid cell.

Among the most highly differentiated of fresh-water algae is *Nitella* (Fig. 43). This is a relatively large plant, several

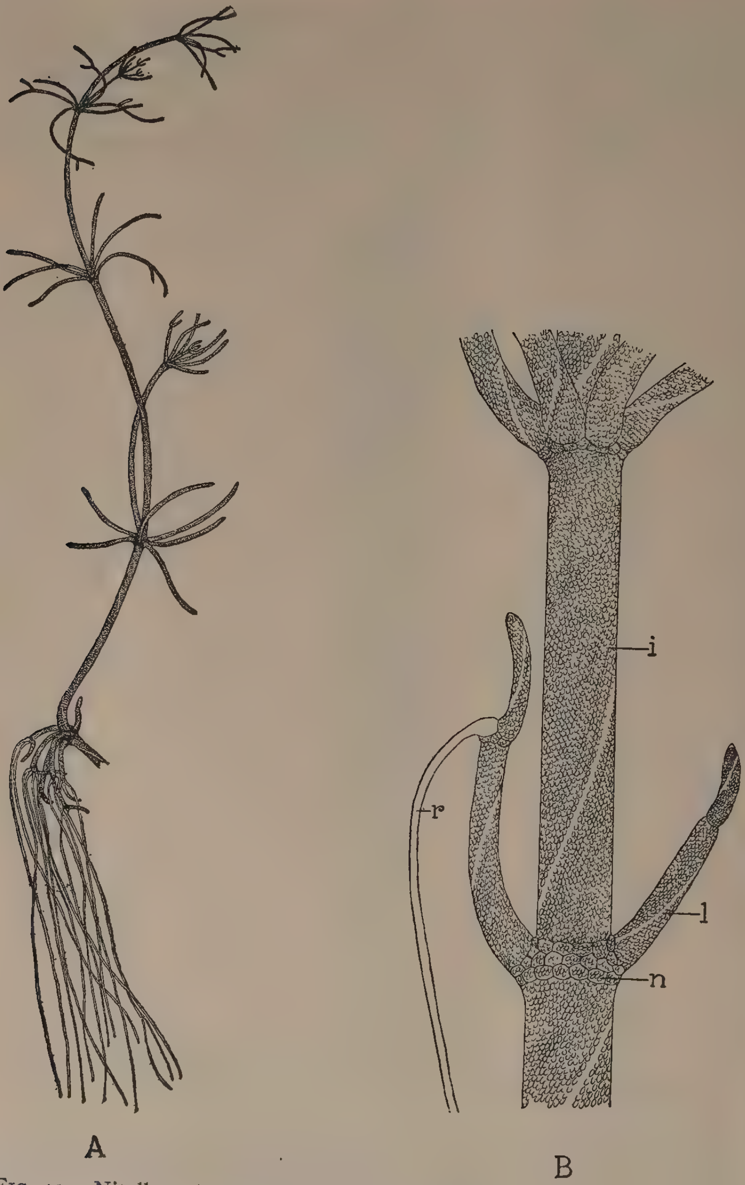


FIG. 43.—Nitella. *A*, whole plant, about natural size. *B*, a small portion magnified. *n*, node; *i*, internode; *l*, "leaf"; *r*, rhizoid.

inches to a foot in length, having a branching green "stem" with regular whorls of "leaves," and colorless rhizoids at the lower end. To the naked eye, this alga strongly resembles some higher plants (seed-plants) growing in the same situations. Microscopic study, however, reveals that its structure is fairly simple. The "stem" consists of long syncytial *internodes* alternating with small multicellular *nodes*. From each node grows a whorl of short branches, similar in structure to the main stem, but of definite and equal size, suggesting "leaves." From some of the nodes also grow long branches like the main stem. From some of the lower nodes originate colorless rhizoids, suggesting "roots," which attach the plant to the soil or rocks at the bottom of the water. Correlated with the structural differentiation of this plant, there is a certain amount of functional differentiation; *i.e.*, of "division of labor" among the different types of cells. The rhizoids serve for *attachment* of the plant to the bottom; being colorless, they are incapable of photosynthesis and must secure organic food substances from the other, green, cells. The "leaves," because of their position and arrangement, are in a particularly favorable situation for absorbing sunlight and therefore for performing *photosynthesis*. The long internodal cells (really syncytia), because of their form and the active circulation of their protoplasm, are well fitted for *distribution* of the synthesized food substances to all parts of the plant. The function of *growth* is also localized in this plant. At the end of each stem and branch there is an *apical cell*, which continually produces new cells by division. These *embryonic* (*i.e.*, small, undifferentiated) cells grow rapidly and differentiate into the various types of cells described above. The branches (stems and "leaves") originate as buds from this *growing point*. This mode of growth is characteristic of practically all multicellular plants.

In some of the larger marine algae (seaweeds), colorless rhizoids, or "holdfasts," are developed as multicellular root-like organs. These rhizoids, however, perform only one of the functions of the roots of higher plants, that of *attachment*. The chief function of true roots—absorption of water and dissolved substances (p. 163)—is, in the algae, performed by every cell for itself. Many of the large seaweeds also develop structures resembling, in external form, the stems and leaves of higher plants; but their internal structure shows little cellular differentiation. In a few of the largest species among the brown algae, the stem shows cellular differentiation comparable to that of the mosses, described below.

Moss.—The mosses belong to a group (bryophytes) comprising the simplest terrestrial green plants. The moss plant (Fig. 44) shows a somewhat higher development and differentiation of nutritive organs than any of the algae. The plant consists of an erect cylindrical stem bearing flat green leaves above ground and colorless rhizoids at its base underground. In aquatic plants, such as the algae, each cell can absorb water and dissolved salts directly from the environment. The moss plant, however, being terrestrial, can absorb these necessary inorganic food materials only through its underground parts, the rhizoids. These rhizoids are fairly simple in structure, consisting of filaments, usually branched, of colorless elongate cells. They are very numerous and often twisted together into stout root-like strands. They serve, like the true roots of higher plants (p. 163), for both *absorption* and *attachment.* Each leaf consists chiefly (in most mosses) of a single layer of cells containing chloroplasts. This structure is well fitted for *photosynthesis*, the chief function of leaves, since each cell is in an advantageous position for absorbing both sunlight and carbon dioxide. The *midrib* of the leaf is several cell layers thick, the extra layers consisting of long narrow cells placed end to end. These elongate cells serve for *distribution* of water and salts to the leaf cells, and of sugars, etc.—the products of photosynthesis—from the leaf to the rest of the plant. Still greater cellular differentiation is found in the stem. In this there are three fairly distinct regions: several layers of green cells on the outside; then a region of loosely packed colorless cells; finally a central cylinder of long slender cells. The outer cells, containing chloroplasts, are capable of photosynthesis. Their chief function, however, is mechanical support and protection of the stem; their cell walls are usually rather thick. The very outermost layer is, in some mosses, especially differentiated in this way, forming a distinct *epidermis.* The thin-walled colorless cells inside these serve chiefly for *storage* of reserve food substances: starch, etc. The empty intercellular spaces among them facilitate *respiration* of the interior cells of the stem. The elongate cells of the central cylinder serve for *distribution* of "raw materials"—water and salts—upward, and of "manufactured" food substances—sugars, etc.—downward through the stem. In some mosses, the end walls of some of these cells are perforated, giving direct

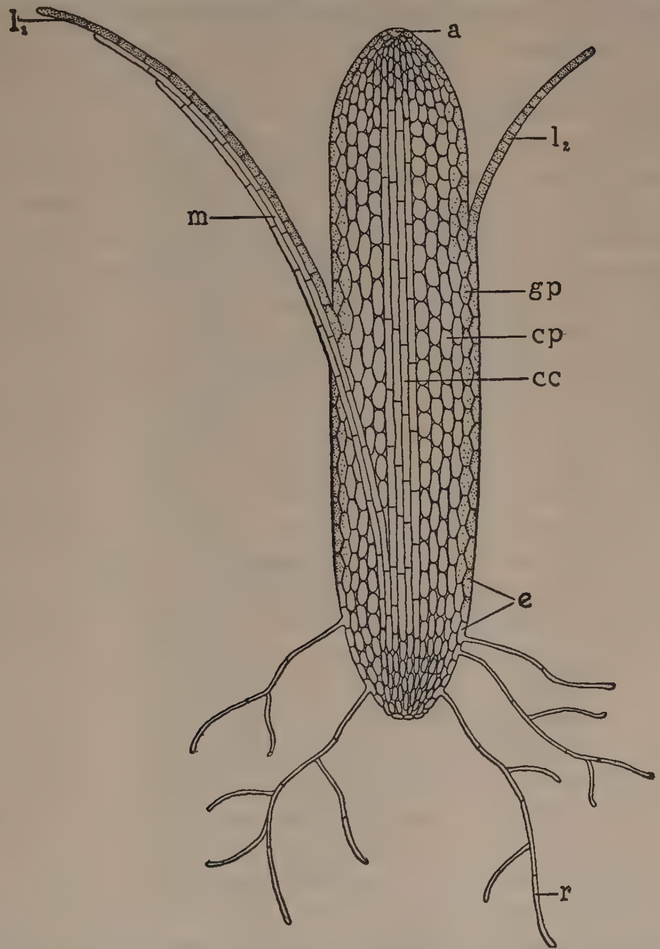


FIG. 44.—Diagram of longitudinal section of moss plant. *a*, apical cell; l_1, leaf cut through the midrib, *m;* l_2, leaf cut through one side; *gp*, green parenchyma; *cp*, colorless parenchyma; *cc*, central cylinder; *e*, "epidermis," scarcely differentiated from the underlying parenchyma; *r*, rhizoid.

protoplasmic continuity from cell to cell, as in the sieve-tubes of higher plants (p. 167). *Growth* is accomplished by the divisions of an apical cell at the end of each stem, as in Nitella. The small cells thus produced grow rapidly and differentiate into the several kinds of cells of the plant. The leaves and branches originate as buds from this growing point of the stem. The rhizoids originate as outgrowths of epidermal cells near the base of the stem.

The moss plant thus has distinctly differentiated multicellular *organs* each specialized for a particular function contributing to the nutrition of the whole organism: the rhizoids for *absorption* of water and salts; the leaves for *photosynthesis;* the stem for *distribution* and *storage* of food substances. Within the stem and leaves there is also considerable cellular differentiation, and, to some extent, a grouping of the different kinds of cells into *tissues.* The types of tissues found in the moss plant—all of which we shall find again, in more highly differentiated forms, in higher plants—may be classified as follows:

(1) *Parenchyma* (relatively undifferentiated cells)
  (a) *Green parenchyma:* cells containing chloroplasts; primary function photosynthesis; in the leaves and outer layers of the stem.
  (b) *Colorless parenchyma:* thin-walled, loosely packed cells without chloroplasts; function chiefly food storage; interior of the stem.
  (c) *Embryonic parenchyma:* small, growing cells, not yet differentiated; tip of the stem.

(2) *Epidermis:* a single layer of cells on the outside of the stem, not very distinctly differentiated in most mosses; functions protection and absorption; the rhizoids may be regarded as specially differentiated epidermal cells.

(3) *Distributing tissue:* elongate cells forming longitudinal strands; function distribution of "raw materials" and "manufactured" food substances; central cylinder of the stem and midrib of the leaves.

Vascular plants.—All plants above the mosses are called *vascular* plants; this designation comprises the pteridophytes (ferns and their allies) and the spermatophytes (seed-plants), all of which are essentially similar in their nutritive mechanisms.

The primary nutritive *organs* of vascular plants are *roots*, *stem*, and *leaves*. The roots are, typically, subterranean and colorless; their primary functions are *absorption* of water and salts and *attachment* of the plant to the soil; in many plants they also serve for *storage* of reserve food substances.

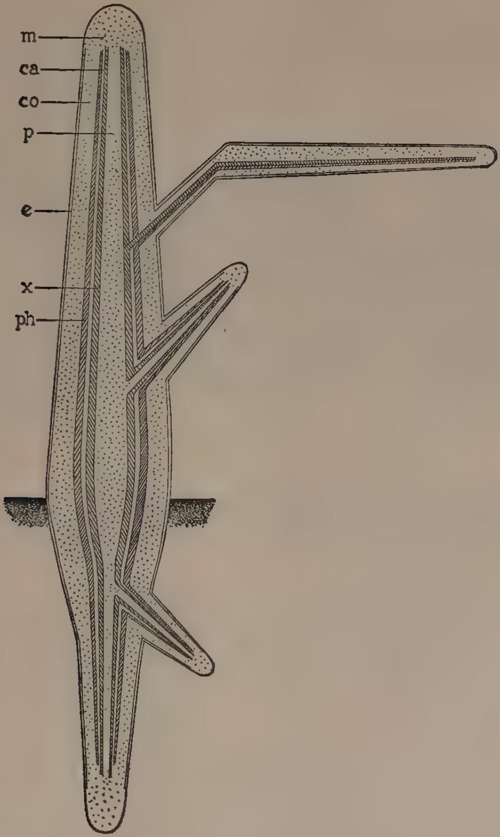


FIG. 45.—Diagram of distribution of tissue systems in a vascular plant (dicotyledon). The diagram represents the main stem and root, each with a small lateral branch, and a single leaf (at the right, above). Fundamental system: *m*, meristem; *ca*, cambium; *co*, cortex; *p*, pith. Epidermal system: *e*, epidermis. Fibro-vascular system: *x*, xylem; *ph*, phloem. (Adapted from Ganong.)

The stem is, typically, erect and above ground; its primary functions are holding the leaves up to the light and *distribution* of food substances between roots and leaves; in many plants the stem also serves for food storage. The leaves are, typically, broad, flat, and green; their primary nutritive function is *photosynthesis.*

Each of these organs is composed of a number of highly differentiated *tissues.* The tissues are classified into three primary *tissue systems:*

(1) *fundamental system:* chief functions photosynthesis, food storage, growth and reproduction.

(2) *epidermal system:* functions protection and absorption.

(3) *fibro-vascular system:* functions distribution and mechanical support.

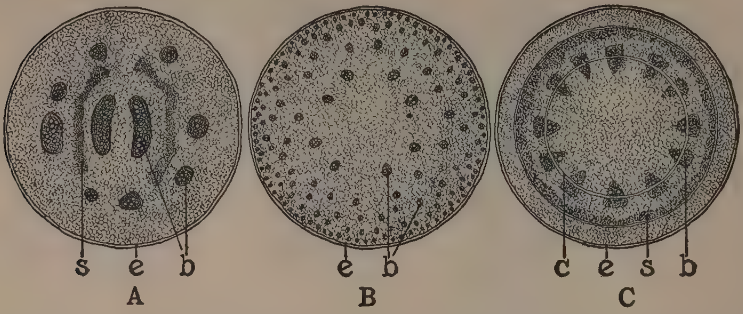


FIG. 46.—Cross sections of stems of three types of vascular plants: *A*, pteridophyte (fern); *B*, monocotyledon (corn); *C*, dicotyledon (young pipe-vine). *e*, epidermis; *s*, sclerenchyma (thick-walled supporting tissue); *b*, fibro-vascular bundles; *c*, cambium.

These three tissue systems extend throughout all parts of the plant; their general distribution is represented diagrammatically in Fig. 45. Each of these tissue systems comprises several distinct types of tissues. We shall describe briefly the structure and arrangement of the more important tissues in each of the nutritive organs, so far as is necessary in order to understand their special functions; beginning with the stem, of which the roots and leaves may be regarded as special modifications.

The *stem* is covered on the outside with a single layer of epidermal cells; its interior is composed of the fundamental tissues (chiefly colorless parenchyma) and a number of *fibro-vascular bundles,* running lengthwise through the stem. These bundles branch and anastomose so as to form a continuous system throughout the stem, roots, and leaves, extending in unbroken continuity from the tips of the roots to the tips of the leaves. This is the most characteristic structural feature of vascular plants; these plants may be said to be "built around" the fibro-vascular system. The arrangement of the bundles in the stem differs in different groups of vascular plants (Fig. 46): in the pteridophytes (ferns, etc.) and the monocotyledons (grasses, lilies, etc.) the bundles are scattered through the interior of the stem; in the dicotyledons (comprising the great majority of higher plants) they are arranged in a regular ring. We shall confine our attention to the latter type (Fig. 47).

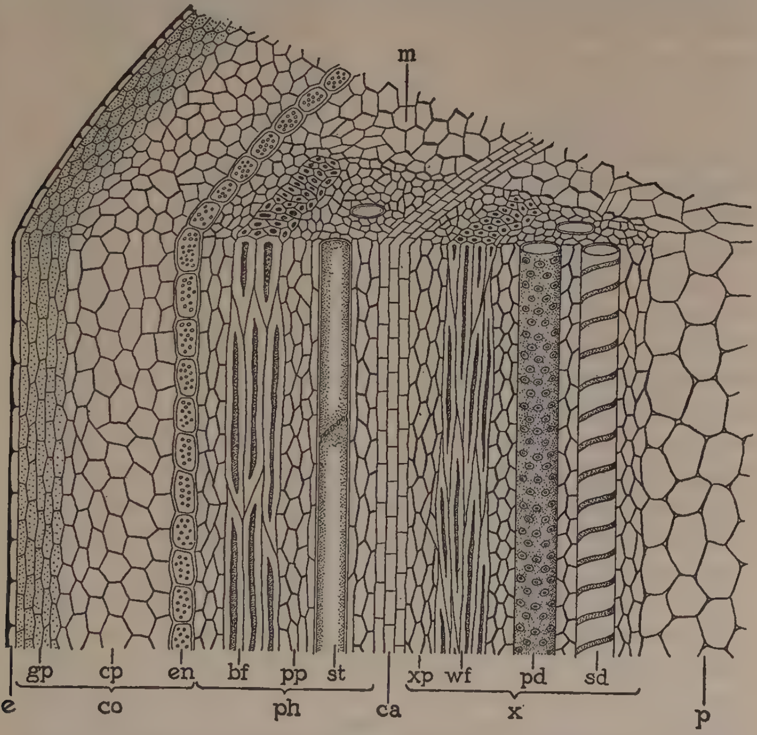


FIG. 47.—Diagram of cross and longitudinal section of portion of a dicotyledonous stem. *e*, epidermis. *co*, cortex: *gp*, green parenchyma; *cp*, colorless parenchyma; *en*, endodermis or "starch sheath," containing numerous starch grains. *ph*, phloem: *bf*, bast-fibers; *pp*, phloem parenchyma; *st*, sieve-tube. *ca*, cambium. *x*, xylem: *xp*, xylem parenchyma; *wf*, wood-fibers; *pd*, pitted duct; *sd*, spiral duct. *p*, pith. *m*, medullary ray.

The epidermis consists of flattened colorless cells, whose walls, especially on the outer side, are somewhat thickened and composed partly of *cutin*, a waxy substance which renders them waterproof. The epidermis protects the underlying tissues from drying, from infection by parasites, and from mechanical injury. The epidermis of young stems usually contains *stomata* like those of the leaf (Fig. 48).

The fundamental tissues of the stem are divided, by the ring of fibro-vascular bundles, into two regions: a central region, the *pith*, and an outer region (between the bundles and the epidermis), the *cortex;* these are connected by strands of tissue, the *medullary rays*, between the individual bundles. The pith, cortex, and rays consist chiefly of *colorless parenchyma*, composed of thin-walled cells, loosely packed, with numerous empty intercellular spaces. The chief function of these cells is storage of reserve food substances, principally starch. The intercellular spaces, which communicate with the outer air through the stomata, facilitate respiration, permitting access of oxygen to, and escape of carbon dioxide from, all the cells of the stem (Fig. 53). The outer layers of the cortex usually consist of elongate, rather thick-walled cells, which aid in mechanical support of the stem; these cells are usually green, containing chloroplasts. The inner boundary of the cortex is formed by a more or less distinct *endodermis*, a single layer of somewhat modified, closely packed, parenchyma cells; everything inside this layer is called the *central cylinder*, comprising the bundles, medullary rays, and pith.

Each fibro-vascular bundle is divided into two regions by a layer of small rectangular cells, the *cambium*, which forms a continuous ring around the stem through the medullary rays as well as the bundles. The inner region of the bundle (between the cambium and the pith) is called the *xylem;* the outer region (between cambium and cortex) the *phloem.* Each of these regions contains *vascular* (distributing) tissues, *fibrous* (supporting) tissues, and parenchyma. The principal types of cells composing these tissues are shown in Fig. 47 and described briefly in the following table.

Xylem (wood):

ducts: long, hollow tubes, composed of cell walls from which the protoplasm which produced them has disappeared; the end walls have also, for the most part, disappeared; the lateral walls are thickened in various patterns (spiral, annular, ladder-like, or pitted), the thickened portions being composed largely of a material called *lignin*, which makes them "woody"; function, the distribution of water and dissolved salts from the roots to other parts of the plant.

tracheids: similar to the ducts, but with oblique, perforated, end walls; found chiefly in the younger portions of the stem (and in the leaves).

wood-fibers: composed of elongate, pointed, overlapping cells with very thick, lignified walls; function, mechanical support.

wood parenchyma: colorless parenchyma, similar to that of the fundamental system.

Phloem (bast):

sieve-tubes: composed of elongate living cells, joining by oblique end walls; the end walls and parts of the lateral walls are perforated by fine pores, giving direct protoplasmic continuity from cell to cell; function, the distribution of organic food substances from the leaves to other parts of the plant.

bast-fibers: similar to the wood-fibers.

bast parenchyma: similar to the wood parenchyma.

The structure of the *root* differs from that of the stem only in minor details. The bundles, which are continuous with those of the stem, usually form a solid central cylinder surrounded by a distinct endodermis. The xylem reaches nearly or quite to the center of the root, and extends between the phloem strands to the endodermis. The cells of the cortex never contain chloroplasts. Near the tip of the root, the epidermal cells have thin uncutinized walls and grow out into *root-hairs* (Fig. 51).

At the tip of each stem and root there is a *growing point* composed of embryonic parenchyma, or *meristem*, cells. Growth in length is effected by the divisions of these cells. Behind the growing point, the embryonic cells rapidly enlarge and differentiate into the various tissues. Leaves and branches originate as buds at the growing point of the stem. Growth in thickness of the stem and root is effected by the divisions of the *cambium* cells; the new cells thus produced enlarge and differentiate into the tissues of the xylem, phloem, and medullary rays. In old stems of many perennial plants—trees and shrubs—the growth of the fibro-vascular bundles, especially the xylem, almost obliterates the cortex and pith, so that the whole stem comes to consist chiefly of wood, *i.e.*, ducts and fibers.

The *leaf* usually consists of a stalk (*petiole*) and a broad, flat portion, the *blade*, which may be either simple or divided into smaller *leaflets*. The structure of the petiole is similar in most respects to that of the stem, described above. The blade (Fig. 48) has numerous branching *veins*, originating either from a *midrib* or directly from the petiole at the base of the leaf. Each vein consists of a single fibro-vascular bundle, with xylem above and phloem below, surrounded by a sheath of elongate parenchyma cells. These bundles are continuous with those of the stem, through the petiole. The bundles of the leaf contain no cambium layer. In the smaller veins, the ducts are replaced by tracheids with spirally thickened walls. The very smallest veins consist of but one or two tracheids and sieve-tubes; before the tip, the sieve-tubes also disappear, and the tracheids finally end among the green parenchyma cells of the leaf.

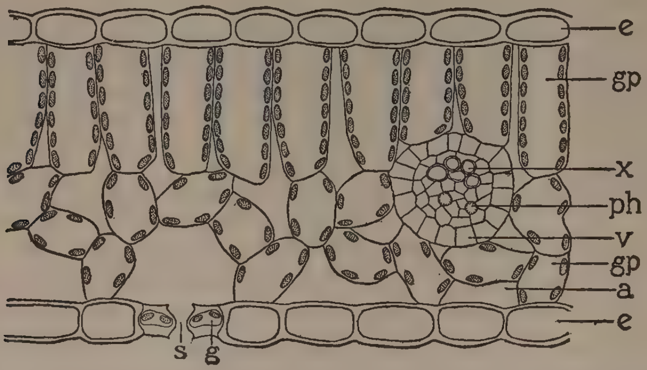


FIG. 48.—Cross section of portion of the blade of a leaf, including a single vein. *e*, epidermis; *gp*, green parenchyma (or chlorenchyma) cells, containing chloroplasts; *a*, intercellular air space; *s*, stoma; *g*, guard-cell. Vein: *x*, xylem; *ph*, phloem; *v*, sheath of vein.

The portions of the leaf between the veins consist of two kinds of tissue: a single layer of epidermal cells on each surface, and several layers of *chlorenchyma* (green parenchyma) cells inside. The epidermis consists of flat colorless cells, with cutinized ("waterproofed") walls. The chlorenchyma consists of thin-walled cells containing numerous small chloroplasts. These cells are loosely packed, leaving large empty intercellular spaces between them, especially in the lower part of the leaf. The intercellular spaces are continuous throughout the leaf, and communicate with the outer air through numerous fine pores, called *stomata*, in the lower surface of the leaf. Each stoma is surrounded by two specialized cells, called *guard-cells*, containing chloroplasts. These guard-cells expand and contract, under certain conditions (p. 174), so as to open and close the stomata. The primary function of the leaf is photosynthesis, which occurs in the chlorenchyma cells. The epidermis serves for protection against drying, infection, and mechanical injury. The veins serve for support, and for distribution of food substances to and from the leaf. The stomata and the intercellular spaces serve for exchange of gases in photosynthesis, respiration, and transpiration (escape of water vapor).

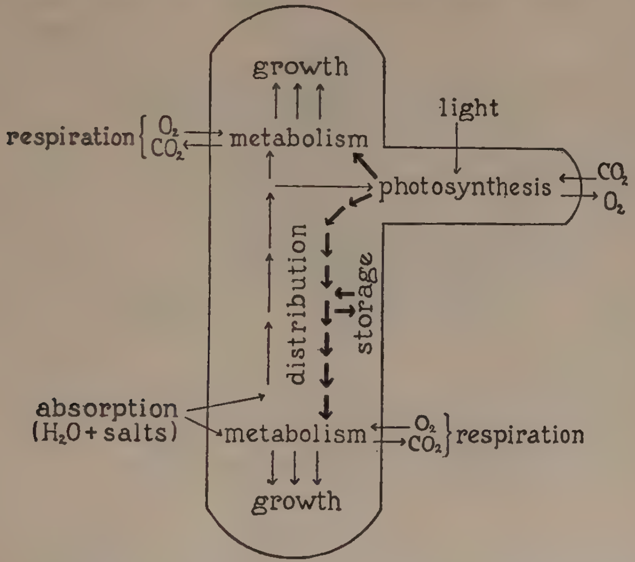


FIG. 49.—Diagram of the nutritive processes of a vascular plant. The vertical part represents stem and root, the horizontal part a leaf. The heavy arrows represent distribution of organic food substances, especially sugars.

Nutrition of vascular plants.—Having learned something of the structure of the specialized nutritive organs and tissues of multicellular plants, we may now proceed to study in more detail the processes of nutrition in a complex, highly differentiated plant. The nutrition of such a plant differs from that of a unicellular green plant (Chapter VIII) only in that some of the accessory nutritive processes are performed chiefly or entirely by specialized types of cells.

The diagram on p. 169 (Fig. 49) represents the interrelations of the various nutritive processes discussed in the following pages.

Absorption of water and salts.—The nutrition of any green plant begins with the absorption of inorganic food materials: carbon dioxide, water, and salts. In a land plant, carbon dioxide is absorbed by the leaves, from the air (p. 176); water and salts by the roots, from the soil. The special absorptive structures of vascular plants are the *root-hairs*, slender cylindrical outgrowths of the epidermal cells of the roots. Root-hairs are confined to a short region, just behind the growing point, of young roots (Fig. 50). Growth in length of the root occurs entirely in front of this root-hair zone; growth in thickness behind it. As the root grows, new root-hairs are being constantly formed behind the growing point; while those further back are constantly dying. Thus the root-hair zone remains short, usually not more than one or two centimeters in length; but within this small region there may be some thousands of root-hairs. The root system of a large plant has, of course, many branches, and therefore many of these young root tips, each with thousands of root-hairs. Each root-hair is only a few millimeters long, but their great number affords an enormous total surface for absorption: the absorptive surface of

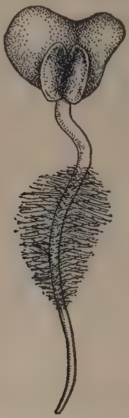


FIG. 50.—Young radish plant (about natural size), showing distribution of root-hairs.

the root epidermis may thus be at least ten or fifteen times as great as it would be without root-hairs.

The root-hair grows at its tip (at or near which its nucleus is located), pushing its way among the minute particles of the soil and adhering closely to them (Fig. 51). Each of these particles is surrounded by a thin film of water, drawn up by capillary force (p. 173) from the "standing water" in the lower levels of the soil. This "capillary water" may amount to from 20% to 300%, in different kinds of soil, of the dry weight of the soil itself. The soil water contains various soluble inorganic salts, including usually all those necessary for the nutrition of green plants (p. 122). These salts come partly from the soluble components of the soil particles, partly from the activities of various bacteria in the soil (Chapter X). The root-hairs themselves may also dissolve some water-insoluble minerals (carbonates, phosphates, etc.) by means of acid substances (chiefly CO_2) which they excrete. This "digestive" action of root-hairs can be readily demonstrated by growing a plant with its roots in contact with a plate of marble ($CaCO_3$): after a few weeks, the marble plate will show an "etching" of the root system of the plant.

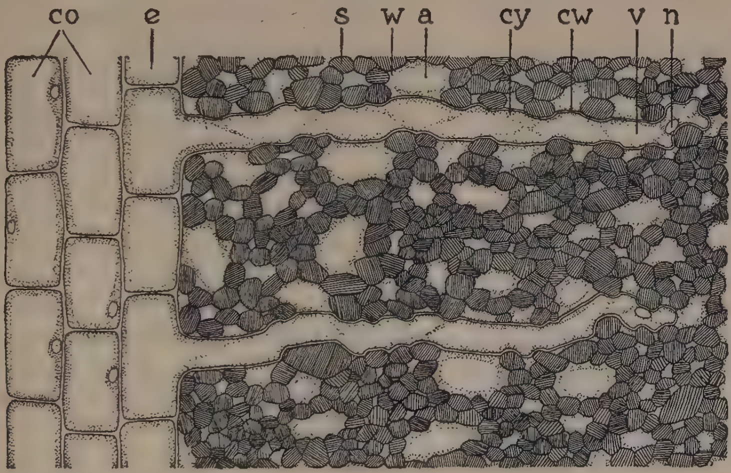


FIG. 51.—Diagram showing relation of root-hairs to the soil. *co*, cortex; *e*, epidermis. Root-hair: *n*, nucleus; *cy*, cytoplasm; *v*, vacuole; *cw*, cell wall. Soil: *s*, soil particle; *w*, water; *a*, air.

The root-hair has a very thin cell wall, inside which is a layer of protoplasm, enclosing a large vacuole filled with cell sap. The cell sap is a relatively concentrated solution of various organic substances, especially sugars. The plasma membrane of the root-hair seems to be impermeable to these substances, so that they do not escape from it. The soil water is a much more dilute solution, so that it is hypotonic to the cell. Therefore, according to the laws of osmosis, this water constantly diffuses into the root-hair. This makes the cell sap of the root-hair more dilute than that of the adjacent cells; water therefore diffuses into these, and so on. At the other end of the plant, water is constantly escaping from the leaves by transpiration (p. 174), and sugars are constantly being made by photosynthesis. Thus the concentration of dissolved substances throughout the plant is maintained above that in the soil water, and water therefore continues to enter the root-hairs by osmosis. The root-hair is also permeable, at least slowly, to some of the dissolved salts in the soil water. Certain of these salts are being constantly used up by the synthetic processes in the plant; these will therefore, according to the laws of diffusion, constantly diffuse into the plant through the root-hairs. Other salts may be absorbed and accumulated in the cells by electrical forces (p. 124).

Distribution of water and salts.—The water and dissolved salts absorbed by the root-hairs diffuse from cell to cell through the cortex of the root to the ducts of its fibro-vascular bundles. Through the ducts, which form a continuous series of tubes throughout the fibro-vascular system of the plant, these substances are carried up through the stem and to every leaf. That this is the path of transfer can be readily demonstrated by placing a cut end of the root of a leafy plant in a water solution of a red dye (*e.g.*, fuchsin): after a day or so, when the dye has appeared in the leaves, longitudinal sections will show that it has passed up through the xylem portion of the bundles of root, stem, leaf-stalk, and veins; microscopic examination will show that it has passed through the ducts.

What are the forces which lift the sap (*i.e.*, water and substances dissolved in it) to the top of the plant—some hundreds of feet in the tallest trees—through ducts which are themselves merely dead tubes of wood? There are several factors involved, including the osmotic activities of the root cells (*root pressure*), *capillarity* in the ducts themselves, and *transpiration* (evaporation) in the leaves.

The first factor is osmotic pressure in the root cells, which keeps water constantly diffusing from the root-hairs inward. The cells are prevented from swelling by their cell-walls, so that this water must escape somewhere. The sap in the ducts is a more concentrated solution than the soil water, since it contains a certain amount of organic solutes (sugars, etc.) diffusing into it from the cells. Thus the whole outer region (epidermis and cortex) of the root forms, in effect, a semi-permeable membrane through which water is drawn by osmotic pressure into the ducts. The osmotic pressure of the cells of ordinary land plants is 10–15 atmospheres,[1] which would be capable of lifting a column of water to a height of 340–510 feet. This osmotic pressure is due chiefly to the sugars dissolved in the cell sap; a 10% solution of glucose has an osmotic pressure of about 12.5 atmospheres. The osmotic pressure of the sap in the ducts is, however, usually much less than this. Direct measurement of the root pressure of certain trees shows that it can raise water to a height of about 80 feet. Root pressure is especially important in the ascent of sap in trees in the spring. At this time the sap contains an unusually great concentration of sugars, resulting from the digestion of starch stored in the root cells (p. 179). Root pressure can be easily demonstrated by cutting off a living plant close to the soil and attaching a vertical glass tube, by a water-tight joint, to the cut end: the sap will be seen to rise in the tube fairly rapidly; *i.e.*, an easily visible amount in a few minutes.

A second factor is *capillary* force in the ducts themselves. This force is familiar in the rise of water in narrow glass tubes; it is due to the intermolecular attractions between the water and the substance of the tubes and among the water molecules themselves. The height to which water will thus rise is inversely proportional to the diameter of the tubes; in wood, in which the ducts are of microscopic diameter (average about 50 μ), water may be drawn up a few feet by capillary force alone. In the walls of the ducts (and of other cells also), where the pores are ultramicroscopic in diameter, this force is even more effective than in their cavities; a considerable amount of water may be thus "soaked up" through the cell walls.

---

[1] 1 atmosphere = the average pressure of the air at sea level = about 15 pounds per square inch, which will lift a column of water about 34 feet.

A third, and ordinarily the most important, factor is the evaporation of water from the leaves, called *transpiration.* Little or no evaporation occurs through the epidermis, because of its cutinized ("waxy") outer cell walls, which make it practically waterproof. But the thin-walled chlorenchyma cells abut everywhere on intercellular air spaces, which are continuous throughout the leaf. Water constantly evaporates from the cells into these intercellular spaces, which communicate with the outer air through the stomata. In most plants stomata occur chiefly or entirely on the under surface of the leaf; in some they are more nearly equal on both surfaces, while in a few (aquatic plants with floating leaves) they occur only on the upper surface. Their number varies from about 40 to 500 per square millimeter of leaf surface in different kinds of leaves. Their average size, when fully open, is about $18\,\mu \times 6\,\mu$. Thus the maximum stomatal opening of a leaf may be as much as 1/20 of its total area. A perforated membrane of this kind, with many small close-set pores, permits a diffusion of gases almost as rapid as though it were an entirely open space. Water therefore evaporates very rapidly from a leaf when the stomata are wide open. The extent of their opening is regulated by the guard-cells. The shape and position of these cells are such that when they are turgid they spring apart, opening the stoma; when they "wilt" they fall together, closing the stoma (Fig. 52). When transpiration exceeds the supply of water to the leaves, the guard-cells, by loss of water from their vacuoles, become less turgid; this automatically closes the stomata, checking further transpiration. The guard-cells, unlike most epidermal cells, always contain chloroplasts; during daylight they manufacture sugars, which increase their osmotic pressure and therefore their turgor; the stomata therefore tend to open in the daytime and close at night. An average amount of transpiration for ordinary plants is 50 grams of water per square meter of leaf area per hour in the daytime, and 10 grams per square meter per hour at night. This is far in excess of the amount of water used for photosynthesis (about 0.6 gram per square meter of leaf area per hour, in the daytime only). Most of the water absorbed by the roots of the plant is therefore merely evaporated by its leaves. But this constantly ascending stream of water serves to carry up the inorganic salts required by the cells much more rapidly than they could travel by diffusion alone. The constant evaporation of water from the leaf cells, and also their constant production of sugars during daylight, keeps their osmotic pressure higher than that of the sap in the ducts. Therefore these cells continually draw water from the ducts and tracheids in the veins, thus creating a negative pressure ("pull") throughout the ducts of the plant. This negative pressure, due to transpiration, can be readily demonstrated by attaching the cut end of a leafy branch to a glass tube containing water. The "pull" of water by transpiration commonly exceeds its upward "push" by root pressure, especially on warm dry days. Under these circumstances, the ducts may not be

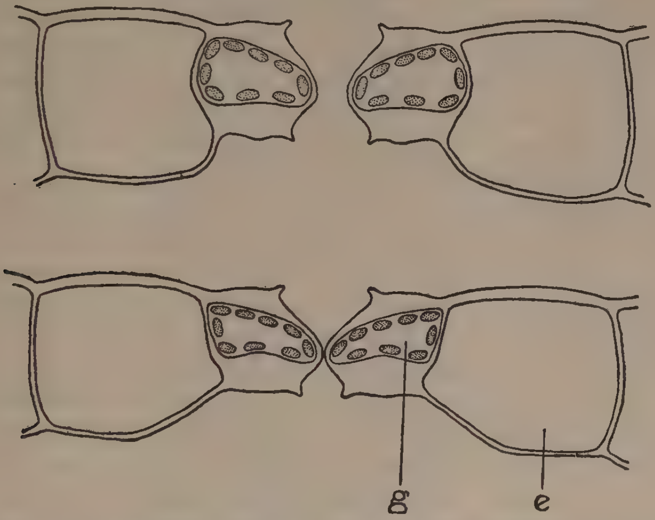


FIG. 52.—Diagrams showing the action of the guard-cells. Above, the guard-cells turgid, leaving the stoma open; below, the guard-cells "wilted" (*i.e.*, less turgid), closing the stoma. *g*, guard-cell, containing chloroplasts; *e*, ordinary epidermal cell, without chloroplasts.

full of sap, but may contain numerous air bubbles, the liquid forming only thin films along the walls of the ducts and between the bubbles. This condition is particularly favorable for the lifting of water by capillarity and by its own cohesive force when pulled from above, since the amount of surface is very large compared to the weight. Under other circumstances, especially at night in the summer, root pressure may exceed transpiration in low plants, so that liquid water is forced out through the stomata.

The height to which water may be lifted, by these several forces in combination, seems to be the chief factor limiting the upward growth of trees; it varies in different species, according to the details of structure of their roots, vascular systems, and leaves. The rate at which the water rises varies, in different plants and under different conditions, from a few centimeters to a meter or more per hour.

Photosynthesis occurs in the chloroplasts of the chlorenchyma cells of the leaves. *Water* is brought to these cells by the ducts and tracheids in the veins; *carbon dioxide* is absorbed from the air in the intercellular spaces, into which it diffuses through the stomata; light is absorbed through the thin transparent epidermis of the upper surface. The chloroplasts are more numerous, and the cells themselves more closely packed, in the upper part of the leaf, where the incoming light is strongest. A single leaf may absorb from 50% to 95% of the light falling on it; the part transmitted and reflected consists chiefly of green waves, ineffective for photosynthesis (p. 126). The light which has passed through one leaf is therefore practically useless to another leaf; but the leaves of a plant are generally so arranged as not to shade each other. Most of the light absorption is done by the chloroplasts, the other parts of the cells being practically transparent; but not more than 4% of the light energy absorbed is actually transformed into chemical potential energy by photosynthesis. The rest is transformed into heat, most of which is dissipated by transpiration; *i.e.*, in changing liquid water into vapor, which absorbs 0.58 Calorie of heat per gram of water evaporated (at ordinary temperatures).

Under ordinary conditions, with good illumination, the principal factor limiting the rate of photosynthesis is the amount of carbon dioxide available. The leaf is capable of utilizing, under these conditions, up to 10% of this gas in the surrounding atmosphere; but only about 0.03% is normally present (p. 122). In daylight, with adequate water supply, the stomata are wide open, and CO_2 is able to diffuse freely into the intercellular spaces, from which it is absorbed by the chlorenchyma cells; the free oxygen produced by photosynthesis diffuses out in the same way.

The chemical reactions involved in photosynthesis have been discussed previously (p. 124). Under natural conditions, the amount of glucose produced by photosynthesis averages about 1 gram per square meter of leaf area per hour, during the daytime. This rate of formation of glucose is much faster than it can be removed by diffusion; the glucose is therefore, according to the laws of reversible reactions (p. 96), synthesized into starch, which is deposited as grains inside the chloroplasts. At night, when photosynthesis is not occurring, the concentration of glucose in the chlorenchyma cells is continually decreasing, by diffusion to other parts of the plant (p. 178); starch is therefore hydrolyzed ("digested") to glucose, by the action of the same enzymes (amylases) which catalyze its synthesis during the day (p. 104). It can be readily demonstrated, by means of the iodine test for starch, that a leaf which contains abundant starch at sunset contains little or no starch the following morning before sunrise.

Synthesis of amino-acids may occur in any living cell of the plant, since it is not dependent on chlorophyl or on light (p. 128). In the higher plants, however, this synthesis seems to occur chiefly in the leaves, where photosynthesis produces an abundant supply of carbohydrate to furnish the matter and energy required. The other necessary elements (N, S) are furnished by the salts brought to the leaf in the sap. The chemical reactions involved have been discussed previously (p. 129). The amino-acids thus produced may be synthesized into proteins in the leaf cells or distributed to the rest of the plant.

Distribution of organic food substances.—Part of the food substances (glucose, amino-acids, etc.) formed in the green leaf cells is utilized for the metabolic processes of these cells themselves. The greater part, however, is distributed to other regions of the plant. The mechanism of this distribution is simple diffusion from cell to cell. The chief path of distribution of these substances is through the sieve-tubes of the fibro-vascular bundles. These, it will be recalled, have direct protoplasmic continuity from cell to cell, which facilitates the process of diffusion; the distribution may also be hastened by protoplasmic movements ("streaming") within these cells. The sieve-tubes have been shown to contain an unusually great concentration of soluble organic food substances (sugars, amino-acids, etc.). Their importance in this respect is also shown by the effects of removing a ring of bark, including the phloem region, from the stem of a plant: the parts below this ring cease to grow, while those above it grow, for a time, more rapidly. Such a plant will, of course, die eventually, because of the death of its roots by starvation.

Through the sieve-tubes, which extend continuously throughout the fibro-vascular system, the food substances manufactured in the leaves are carried downward to the stem and roots, and upward to the growing points of the stem and branches. Their upward transport may be also, in part, effected by the ascent of sap in the ducts. The distribution of these foods—as well as of water and salts—inward and outward through the stem, to the pith and cortex, is effected chiefly by the medullary rays, whose cells are usually elongated horizontally and have pitted walls.

Storage of food.—During the summer, when photosynthesis and other synthetic processes are proceeding actively, the amount of food produced exceeds the immediate requirements of the plant for matter and energy. This excess food is *stored* in various parts of the plant. A large part is stored in seeds and fruit, structures concerned in reproduction (Chapter XXI). In all plants which live more than one year, a considerable portion is also stored in the nutritive organs, especially the stem and roots. The chief places of food storage are the colorless parenchyma cells in the cortex, pith, medullary rays, and within the xylem and phloem regions of the bundles. In many plants there are special storage organs; *e.g.*, fleshy roots, tubers (modified underground stems), specialized thickened leaves, etc.

The most abundant stored food in most plants is *starch*.

This is always stored in the form of grains, which differ characteristically in size, form, and markings in different plants (Fig. 15). These grains are formed in special plastids (*amyloplasts*), which are colorless and smaller than chloroplasts. Some plants store a special, easily digestible, form of cellulose (*hemi-cellulose*), which is deposited on the inside of the cell walls. Other plants store *sucrose*, dissolved in the cell sap. *Fats* occur more frequently in seeds (*e.g.*, nuts) than in the nutritive organs; they may be in the form of liquid droplets (oils) or of crystals (solid fats); in some cases they seem to be formed by special plastids (*elaioplasts*). Stored *proteins* occur, especially in seeds, in the form of granules and crystals.

These substances are synthesized, in the cells of the storage tissues, from simpler food substances (sugars, amino-acids, etc.) during the summer. The chemical reactions involved have been discussed previously (pp. 116, 130). During the winter, all the metabolic processes of the plant proceed very slowly, due to the low temperature (p. 95), so that very little of the stored food is used up. In the spring, the higher temperature increases both the rate of water absorption and the activity of the enzymes in the cells (p. 99). The stored food substances are then hydrolyzed and carried, largely in the sap, to the growing points, where rapid growth, especially of leaves, then occurs.

General metabolism.—The essential processes of metabolism, to which all the other nutritive processes are accessory, occur in *every living cell* of the plant. The various chemical reactions involved in metabolism, and their inter-relations, have been discussed previously (Chapters VII, VIII). As we have noted (p. 132), the *destructive* metabolism in plants is usually relatively much less than in animals, because the plant expends much less energy in movement. In rapidly growing plant tissues, however, the rate of oxidation may equal or exceed, weight for weight, that of even a warm-blooded animal. The amount of organic substance (chiefly carbohydrate) oxidized by an adult man is, roughly, about 1% of his body weight per day; in rapidly germinating seeds of some plants, it may amount to 3% of their weight per day. This high rate of oxidation supplies the energy required for growth; *i.e.*, for the "uphill" chemical reactions as well as the physical processes (cell division, etc.) involved in growth. In an older plant, in which the amount of growing tissue is relatively small, the rate of oxidation, for the plant as a whole, is very much smaller.

The *constructive* metabolism of the plant cells includes the synthesis of reserve food substances, of the components of protoplasm, and of cell-wall materials (cellulose, lignin, etc.). The formation of protoplasm—*assimilation*—occurs chiefly in the embryonic cells of the growing points and cambium layer. The formation of skeletal (cell-wall) materials occurs chiefly in the cells just behind the growing points and those on either side of the cambium layer, which are differentiating into their final forms as ducts, fibers, etc.; in the mature plant a very large proportion of its total bulk consists of these dead cell-wall materials. Plant cells also produce a great variety of other, more or less complex, organic substances (p. 131), which may serve various accessory functions or be merely by-products of metabolism.

The following estimate has been made of the proportions of the total *organic* matter synthesized by the plant which are used in these various ways. These proportions would, of course, differ greatly in different kinds of plants and at different stages of their lives; the estimate, which is necessarily very rough at best, refers to an "average" seed-plant in the mature stage.

	Per Cent
Destructive metabolism (oxidation)	15
Stored foods	50
Skeletal (cell-wall) materials	25
Organic components of protoplasm (chiefly proteins)	5
Other organic substances	5

These figures serve to emphasize, in particular, two points: the relatively large amount of lifeless skeletal and food materials in the higher plants, as compared with the amount of living protoplasm (the latter, however, contains a much larger proportion of water); and the relatively small proportion of the plant's food used in destructive metabolism, as contrasted with the large proportion so used in animals (Chapter XII).

Respiration.—Every living cell of the plant continuously consumes O_2 and produces CO_2, in its destructive metabolism. The green cells of the leaf, during daylight, liberate more than enough free oxygen for their own oxidative requirements, and consume more CO_2 than they produce (p. 133). But the cells of the stem and root, and the leaf cells at night, must obtain oxygen from outside and get rid of carbon dioxide. This exchange of gases is effected through the intercellular spaces, which form a continuous series of air passages throughout the parenchymal tissues of the plant, opening to the outer air through the stomata (Fig. 53). The roots have no stomata, but exchange oxygen and carbon dioxide with the air spaces in the soil by diffu-

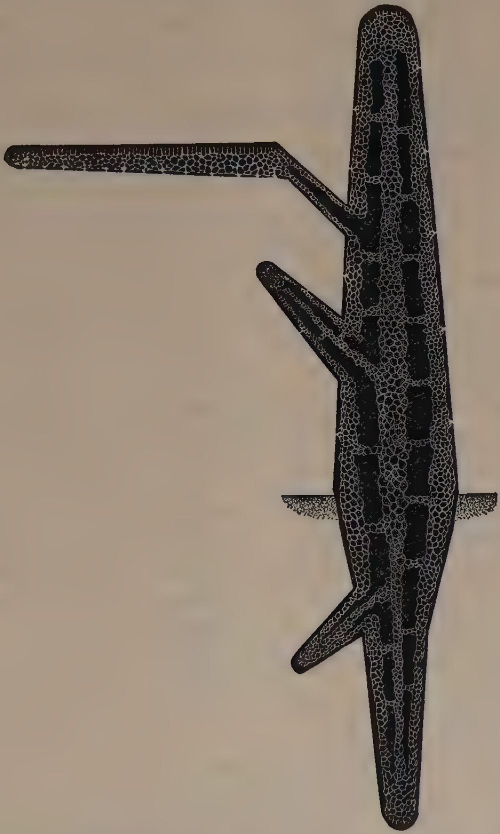


FIG. 53.—Diagram of the aeration system of a vascular plant (dicotyledon). Compare with Fig. 45. The white lines represent intercellular air spaces, opening to the outside through stomata. (Adapted from Ganong.)

sion through the root-hair cells. In good soil, from 20% to 40% of the volume of the soil consists of minute air spaces among the soil particles (Fig. 51). The oxygen in these spaces dissolves in the water films surrounding the soil particles and root-hairs, and diffuses through the root-hairs into the intercellular spaces of the root; carbon dioxide diffuses out in the same way. There is no mechanism for circulation of these gases through the plant, except the slow process of diffusion. This is not efficient enough to accomplish an adequate distribution through any considerable distance within the plant; so each part of the plant must "breathe" for itself. Thus the roots may be killed if the soil be so tightly packed as to exclude air. If the soil becomes saturated with water, the roots will be drowned, just as an air-breathing animal would, except that it would take longer to drown the plant because its oxygen requirement is smaller. Similarly, the stem may be killed by packing soil tightly about it, even though the leaves be exposed.

Excretion.—The chief waste products of plant metabolism are H_2O, CO_2, and O_2 (in photosynthesis). The methods of removal of these substances have already been discussed; whether these processes are to be called "excretion" is purely a question of words. Aside from these, there is very little excretion by plants, because their other waste products (especially those containing nitrogen) are used up again in synthetic processes (p. 133).

The roots, as previously noted (p. 171), commonly produce acidic solutions, but this acidity is due chiefly to carbon dioxide (p. 42). They may also excrete small amounts of other acids (*e.g.*, lactic acid), but this question is in dispute; the excretion of lactic acid, and perhaps other organic acids, might occur under conditions of inadequate oxygen supply (p. 119). Many flowers and some leaves have special gland-cells (p. 274) which secrete a mixture of sweet and odorous substances, called *nectar*, perhaps to be regarded as waste products. Other waste products accumulate in insoluble forms, often in special cells; one of the most frequent is calcium oxalate, an insoluble crystalline salt, whose deposition serves to remove oxalic acid, a toxic by-product of metabolism. These crystals often occur in the leaves and bark, whose shedding and wearing serve to excrete them. The pigments of flowers and autumn leaves are also, probably, chiefly waste products. In regard to all these and many other substances produced by plants, it is very difficult to determine whether they are simply waste products or may have some useful function in the life of the plant. In the latter case, they might be called "secretions" rather than "excretions"—but this is a rather arbitrary distinction.

Summary of nutritive mechanisms of green plants.—

	Unicellular and simple colonial algae	*Nitella*	*Moss*	*Vascular plants*
Absorption	by every cell directly	by every cell directly	rhizoids	root-hairs
Distribution	intracellular diffusion	large internodal cells	elongate cells in center of stem and midrib of leaf	ducts and tracheids; sieve-tubes; medullary rays
Photosynthesis	chloroplasts in every cell	every cell except rhizoids	chlorenchyma cells of leaf and stem	chlorenchyma cells of leaf (and young stem)
Storage	in every cell	in every cell	colorless parenchyma cells of stem	colorless parenchyma cells of stem and root
Metabolism	in protoplasm of every living cell			
Respiration	diffusion directly to and from surrounding water	diffusion directly to and from surrounding water	diffusion directly to and from surrounding air; through outer cells and air spaces in stem	through stomata and root-hairs, and intercellular air spaces
Excretion	diffusion directly to surrounding water	diffusion directly to surrounding water	rhizoids; deposition of insoluble substances in cells	root-hairs; gland-cells; deposition of insoluble substances, often in special cells

CHAPTER XII

NUTRITIVE MECHANISMS OF MULTICELLULAR ANIMALS

Among animals we find no such gradual transition from unicellular to multicellular forms as among the lower plants. Most of the protozoa are strictly unicellular; in those which are colonial, there is practically no differentiation among the cells, each cell performing all the processes of nutrition (and all other life processes) for itself. There is thus a sharp line of demarcation between the protozoa—unicellular and colonial animals—and the *metazoa*—multicellular animals. In even the simplest metazoa there is considerable differentiation among the cells and a grouping of these cells into *tissues*. From these to the highest animals, however, there are further increases in complexity and differentiation, not only of tissues but also, to a much greater extent than in plants, of localized *organs*. We shall examine briefly the nutritive organs of a series of animals representing successive "steps" of increasing complexity from the simplest multicellular animals to the most complex, and then, in more detail, the nutritive mechanisms of the "highest" group of animals, which includes man.

Hydra, the Fresh-water Polyp (Fig. 54), is one of the simplest multicellular animals. Its body is a hollow cylinder, composed of two layers of cells, with an opening, the *mouth*, at one end, leading into the digestive cavity, or *enteron*. This fundamental feature of body structure—an internal hollow digestive cavity, communicating with the exterior through an ingestive opening—is common to practically all multicellular animals. While the higher plants are "built around" the fibro-vascular system (p. 165), multicellular animals are "built around" the digestive system. Thus the animal body is fundamentally a *hollow* structure (Fig. 57), while that of the plant is, in its gross structure, solid (Fig. 45).

Hydra shows considerable cellular differentiation, with various kinds of cells specialized for particular functions. These cells are grouped into two *tissues: ectoderm* (outer layer) and *endoderm* (inner layer). The tissues are less differentiated than those of higher animals, since each layer contains several kinds of cells, some of which are just alike in both layers. The ectoderm consists chiefly of small, close-set *epithelial cells*, extended at their inner ends into elongate contractile *muscle-processes* (p. 247). Scattered among these epithelio-muscular cells there are smaller numbers of specialized *sensory cells*, *nerve-cells*, and *nettle-cells*. Between the bases of the epithelial cells are many small, undifferentiated, embryonic cells, called *interstitial cells*, which multiply, grow, and differentiate into the various kinds of ectoderm cells. The endoderm consists chiefly of

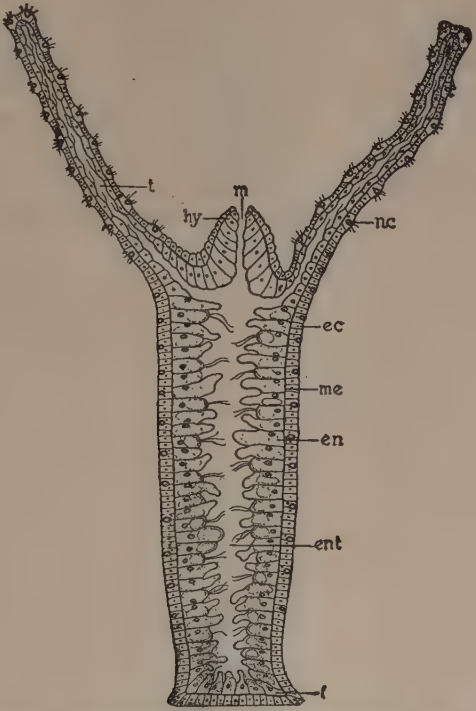


FIG. 54.—Hydra, longitudinal section. *ec*, ectoderm; *en*, endoderm; *me*, mesogloea; *ent*, enteron; *m*, mouth; *hy*, hypostome; *t*, tentacle; *f*, foot; *n.c.*, nettle-cell.

larger epithelial cells, having both flagella and pseudopodia at their free ends, and muscle-processes at their basal ends. The endoderm also has interstitial cells, sensory cells, and nerve cells, like those of the ectoderm, and specialized *gland-cells* which secrete mucus and digestive enzymes. Between the ectoderm and the endoderm is a very thin, transparent layer of intercellular substance, the *mesogloea.*

Hydra also has localized multicellular *organs*, though these also are less differentiated than in higher animals. The *mouth* is at the summit of a conical elevation, the *hypostome*, at one end of the body. Surrounding this is a ring of long *tentacles*, which are hollow, containing extensions of the enteric cavity. The opposite end of the body is somewhat differentiated as the *foot*, serving for attachment and crawling.

The *food* of the hydra, which consists chiefly of small swimming animals, is captured by the nettle-cells. These "explode" on contact and discharge long poisoned threads which pierce and paralyze the prey. The food is then pulled in by the tentacles and *ingested* through the mouth. *Digestion* is partly *extracellular*, in the enteric cavity, by the action of hydrolyzing enzymes secreted by the gland-cells; but chiefly *intracellular*, as in protozoa. Small food particles are ingested by the pseudopodia of the endoderm cells, just as in Amoeba, and digested in food vacuoles. Indigestible materials are *egested* through the mouth, which is the only opening of the enteric cavity. The endoderm cells *absorb* the digested food substances from the enteron and from the food vacuoles. The ectoderm cells get their nourishment by diffusion from the endoderm cells. *Respiration* and *excretion* are effected by diffusion from and to the surrounding water, as in protozoa.

Planaria (Figs. 55, 56), a common fresh-water flatworm, has a much greater resemblance than Hydra, in its general body form, to the more familiar higher animals. It has differentiated *anterior* and *posterior* (front and hind) ends, and *dorsal* and *ventral* (upper and lower) sides. In its internal structure it also shows much greater tissue and organ differentiation than Hydra. Between the ectoderm on the outside and the endoderm lining the digestive cavity, it has a number of other tissues called collectively the *meso-*

derm. The mesoderm of Planaria consists chiefly of undifferentiated *parenchyma* with irregular intercellular spaces. These intercellular spaces do not contain air, as in plants, but a colorless *body-fluid*, consisting chiefly of water with dissolved food and waste substances. The outer part of the mesoderm, next to the ectoderm, is differentiated as *muscle* tissue. Embedded in the parenchyma are the highly differentiated *nervous*, *reproductive*, and *excretory* systems.

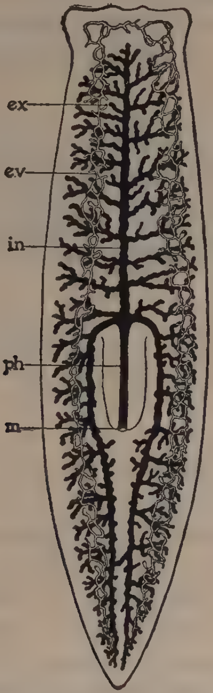


FIG. 55.—Planaria, digestive and excretory systems. *m*, mouth; *ph*, pharynx; *in*, intestine; *e.v.*, excretory vessel; *ex*, excretory pore.

The *mouth* is on the ventral surface, nearer the posterior end of the animal. It opens into a cylindrical muscular tube, the *pharynx*, which can be protruded as a proboscis; by means of this organ the planaria secures and ingests its food. The pharynx opens into the *intestine*, the main portion of the enteron. The intestine is complexly branched, ramifying throughout the body. *Digestion* is chiefly extracellular, in the cavity of the enteron, by the action of hydrolyzing enzymes secreted by gland-cells in the endoderm; partly intracellular, within the endoderm cells. Indigestible residues are egested through the mouth, which is the only opening of the enteric cavity. The branching form of the intestine effects the distribution of food to all parts of the body; after digestion and absorption by the endoderm cells, the dissolved food substances pass by diffusion through the body-fluid to the mesoderm and ectoderm cells. *Respiration* is also effected by diffusion, through the ectoderm and the intercellular fluid.

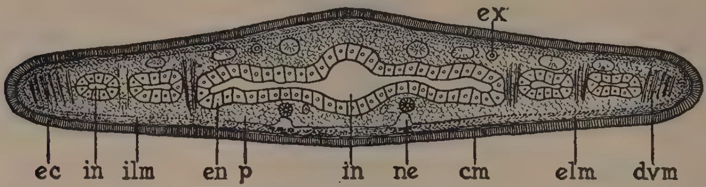


Fig. 56.—Planaria, cross-section. *ec*, ectoderm; *en*, endoderm; *in*, intestine; *p*, parenchyma; *cm*, circular muscles; *elm*, *ilm*, external and internal longitudinal muscles; *dvm*, dorso-ventral muscles; *ne*, nerve cord; *ex*, excretory vessel. The other, unlabelled, organs embedded in the parenchyma are parts of the reproductive system.

There are special organs for *excretion*. These consist of a pair of long coiled tubes, joined at the anterior end, and opening on the dorsal surface by minute pores. Each of these tubes is composed of hollow cylindrical cells placed end to end. These tubes branch complexly, the terminal branches ending in *flame-cells*. The flame-cell is a large hollow cell with a bunch of long *cilia* extending into its central cavity, which communicates with the cavity of the excretory vessels. The waste products of metabolism diffuse from the body fluid into the flame-cells and excretory vessels; the cilia of the flame-cells keep a current of water flowing outward through these tubes. This system probably serves, like the contractile vacuoles of fresh-water protozoa, to excrete excess water which enters the body by osmosis, as well as the waste products of metabolism.

Earthworm.—The common earthworm exhibits, very clearly, the general structural features common to all animals above the flatworms (Fig. 57). Compared with Planaria, the earthworm shows a number of significant advances in tissue and organ differentiation. The mesoderm, instead of being largely parenchymous as in the flatworms, is entirely differentiated into specialized tissues, chiefly *muscle.* This muscle tissue, which constitutes the chief bulk of the animal, is divided into two separate layers: a very thick one, next to the ectoderm, forming the *body-wall;* and a thinner layer, next to the endoderm, forming the wall of the enteron. Between these two muscle layers is a continuous *body-cavity*, called the *coelom.* This cavity completely surrounds the enteron and all the other internal organs. It is lined by a layer of epithelial cells, the *peritoneum*, and filled with a colorless body-fluid (*coelomic fluid*).

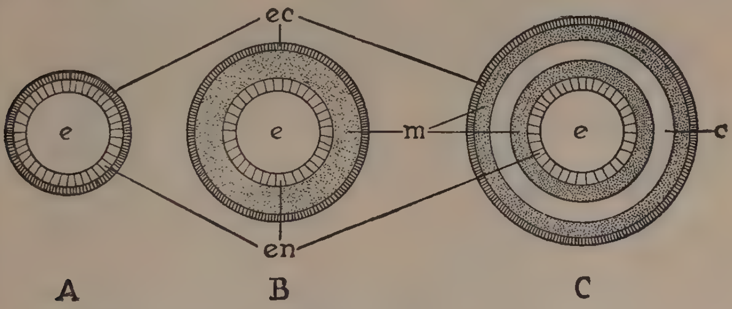


FIG. 57.—Diagrams of cross-sections of (*A*) Hydra, (*B*) Planaria, (*C*) earthworm. *ec*, ectoderm; *en*, endoderm; *m*, mesoderm; *e*, enteron; *c*, coelom.

The earthworm is *segmented* ("jointed")—another feature common to many, though not all, higher animals. This segmentation is indicated externally by grooves around the body at regular intervals; internally by transverse *septa* (partitions) dividing the coelom into a series of almost separate annular cavities. Many of the internal organs are repeated in each segment. Externally, most of the segments look exactly alike; internally, there is a certain amount of differentiation among the more anterior segments, but those of the posterior two-thirds (or more) of the body are practically identical.

The *enteron* has the form of a tube, running lengthwise through the body, and open at both ends. It is variously differentiated, in different regions, into specialized organs (Fig. 59). The *mouth* is on the ventral side of the first segment. The earthworm swallows everything in front of it as it burrows through the soil; its food consists of all the digestible substances contained in this dirt. The mouth opens into the *mouth cavity* (segments 1–3); this opens into the thick-walled, muscular *pharynx* (segments 4–5). The pharynx acts as a "suction pump" by which dirt and food materials are sucked in through the mouth. The pharynx opens into a straight cylindrical tube, the *esophagus* (segments 6–14). Three pairs of multicellular glands, the *calciferous glands* (segments 10–12), secrete calcium carbonate into the esophagus; this may be purely a waste substance, or may serve to neutralize acids in the food. The esophagus opens into the *crop* (segments 15–16), a thin-walled, very distensible sac, in which the ingested materials accumulate and pass along gradually into the *gizzard* (segments 17–18), a thick-walled, muscular organ by which the food is ground up finely. The remainder of the enteron is the *intestine*, extending straight from the gizzard to the posterior end of

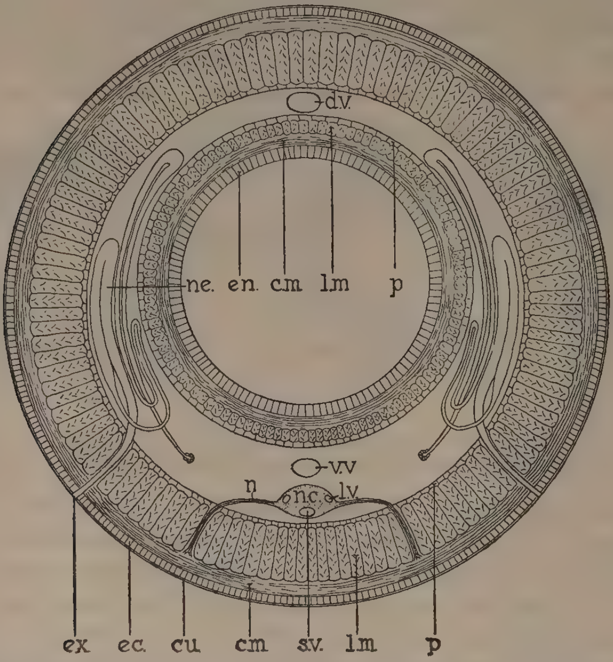


Fig. 58.—Earthworm, diagrammatic cross-section. *ec*, ectoderm; *cu*, cuticle (non-cellular layer secreted by the ectoderm); *cm*, circular muscles; *lm*, longitudinal muscles; *p*, peritoneum; *en*, endoderm; *ne*, nephridium; *ex*, excretory pore; *n.c.*, nerve cord; *n*, nerve; *d.v.*, dorsal blood-vessel; *v.v.*, ventral blood-vessel; *s.v.*, sub-neural blood-vessel; *l.v.*, lateral-neural blood-vessel.

the worm, where it opens to the outside through the *anus*. *Digestion* is entirely (or almost entirely) *extracellular*, occurring in the cavity of the intestine, by the action of hydrolyzing enzymes secreted by gland-cells in the endoderm lining the intestine. The digested food substances are *absorbed* by the endoderm cells. The indigestible residues are egested through the anus.

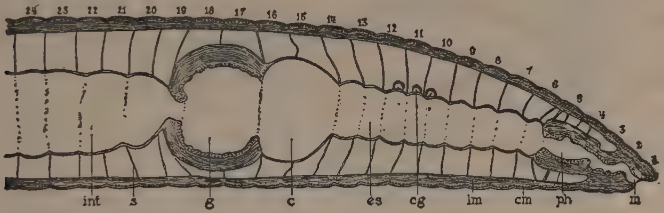


FIG. 59.—Earthworm, anterior portion of the digestive system in longitudinal section. *m*, mouth; *ph*, pharynx; *es*, esophagus; *cg*, calciferous gland; *c*, crop; *g*, gizzard; *int*, intestine; *s*, septum. The numbers indicate the segments; all the posterior segments are similar to the last ones shown.

In the earthworm, as in practically all animals above the flatworms, *distribution* of the absorbed food substances is effected by a special system of organs, the *circulatory* or *blood-vascular* system. This system consists of a continuous series of tubes, the *blood-vessels*, ramifying throughout all parts of the body, and containing a fluid tissue, the *blood*. The blood consists of a liquid intercellular substance, the *plasma*, and the *blood cells*. The plasma is a dilute solution of salts, dissolved food and waste substances, and proteins. Most important of the blood proteins is *hemoglobin*, which gives the red color to the blood and plays a very important rôle in the transportation of oxygen (p. 226). The blood cells are mobile cells, very similar to amoebae, which crawl about in the blood vessels and also in the body cavity and intercellular spaces. The plasma carries soluble food and waste substances in solution; the blood cells aid in the transportation of insoluble food substances (*e.g.*, fats) and waste materials (such as the debris of dead cells) and also in the protection of the organism against parasites, especially bacteria.

The larger blood vessels of the earthworm are five longitudinal vessels running throughout its length, connected by transverse vessels in each segment. The blood is propelled

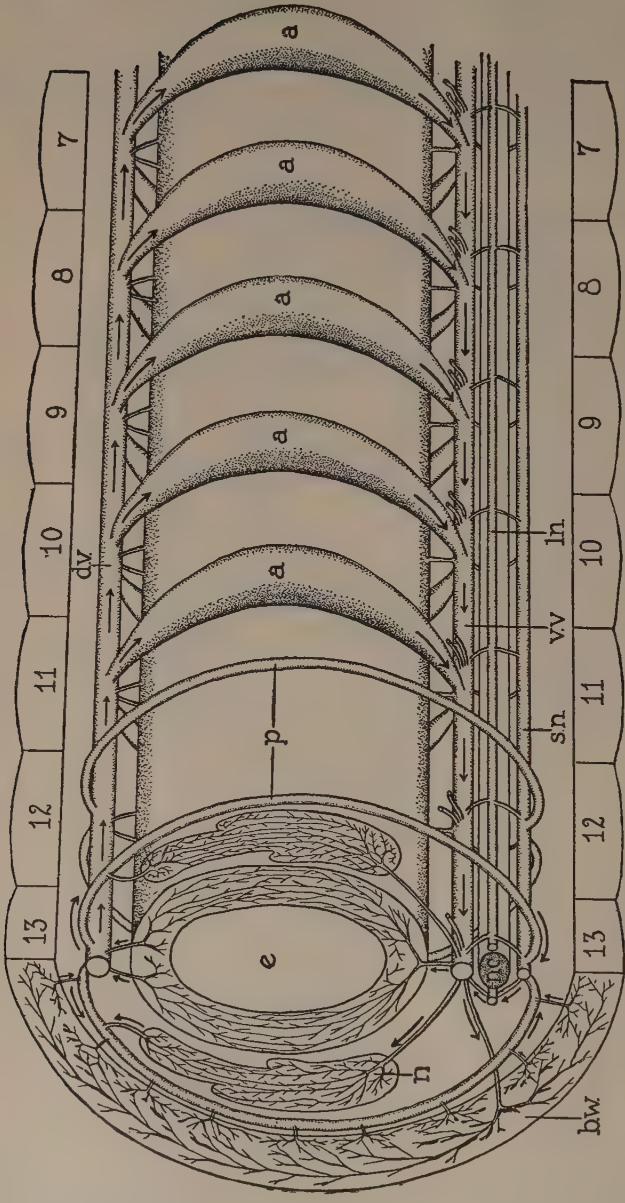


FIG. 60.—Diagram of the circulation of the blood in the earthworm; the arrows indicate the direction of flow of the blood (there is, however, considerable doubt about some of the details). *d.v.*, dorsal vessel; *v.v.*, ventral vessel; *s.n.*, subneural vessel; *l.n.*, lateral-neural vessel; *a*, aortic arches; *p*, parietal vessels; *e*, enteron; *b.w.*, body-wall; *n*, nephridium; *n.c.*, nerve cord. The numbers indicate the segments; all the posterior segments are similar to the last one shown; segments 1–6, and many details in segments 7–12, are omitted from the diagram.

by rhythmic contractions of the longitudinal *dorsal vessel*, and of the transverse *aortic arches* in segments 7–11. The direction of flow is always forward in the dorsal vessel and downward in the aortic arches; this direction is determined by *valves* inside these vessels, which prevent flow in the opposite direction, and also by the timing of the contractions of the dorsal vessel, which run forward as "waves" starting at the posterior end. From the aortic arches the blood runs backward in the longitudinal *ventral vessel*. From this vessel branches are given off, in each segment, to the body-wall, the wall of the intestine, and the excretory organs. These branches divide and subdivide, forming finally a multitude of very fine, thin-walled vessels, the *capillaries*, which extend as a continuous network throughout all the organs of the body. The capillaries reunite to form larger vessels, which open into some of the main longitudinal and transverse vessels; through these the blood eventually returns to the dorsal vessel. The course of the blood is thus a *closed circulation; i.e.*, the blood remains always inside the blood vessels, in which it pursues a "circular" course over and over. In the thin-walled capillaries, however, the blood effects osmotic exchanges with the body-fluids of the coelom and intercellular spaces, and these in turn with the cells. In this way the blood acts as a medium of *food distribution*, of *respiration*, and of *excretion*.

In the wall of the intestine, just outside the endoderm layer, is a rich network of capillaries. Through their very thin walls, the absorbed food substances (sugars, amino-acids, etc.) diffuse from the endoderm cells into the blood. In the blood these substances are distributed to all parts of the body, where they diffuse from the capillaries to the intercellular spaces and thence into the cells.

Respiration, in animals with a blood-vascular system, comprises three distinct processes: *external respiration*, the exchange of O_2 and CO_2 between the blood and the external environment (air or water); *transportation* of these gases by the blood; and *internal respiration*, the exchange of O_2 and CO_2 between the blood and the cells. By *respiratory organs* we always mean the special organs of external respiration. The earthworm has no specialized respiratory organs, but the whole skin (ectoderm) serves as such. The skin is richly supplied with blood capillaries. Its surface is kept moist by mucus secreted by gland-cells in the ectoderm. Through this moist skin, oxygen diffuses from the outer air

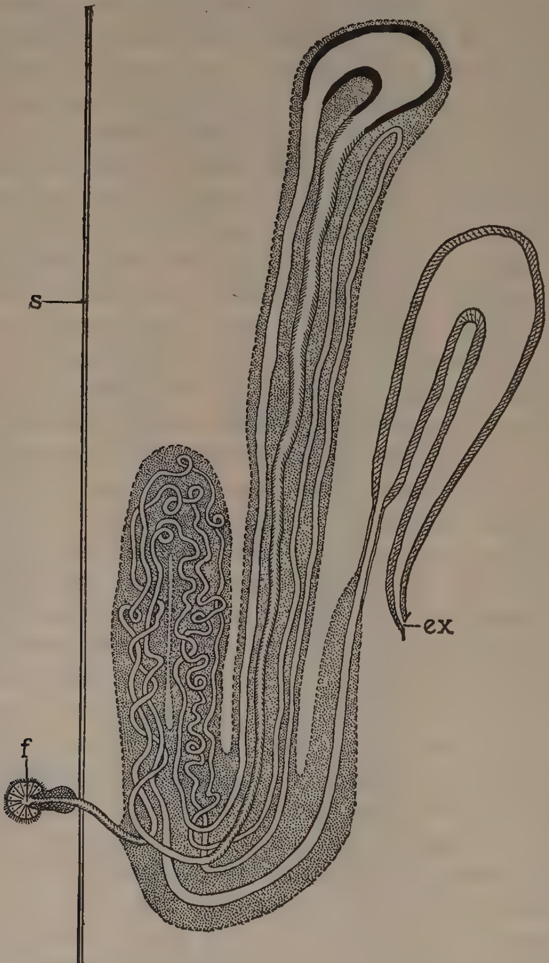


FIG. 61.—A nephridium of the earthworm. *f*, ciliated funnel opening from the coelom; *s*, septum; *ex*, excretory pore opening to the outside of the body.

into the blood in the capillaries, and carbon dioxide diffuses from the blood to the air. Oxygen is transported by the blood chiefly in chemical combination with hemoglobin; carbon dioxide chiefly in combination with sodium as sodium bicarbonate (p. 227). In the various tissues of the body, oxygen diffuses from the blood to the intercellular spaces and thence into the cells; carbon dioxide diffuses in the opposite direction. The directions of these diffusions are determined by the differences in concentration of these gases between the cells, where O_2 is being continually consumed and CO_2 produced, and the outer air, where O_2 is much more abundant than CO_2; the concentrations of these gases in the blood are intermediate between their concentrations in the cells and in the outer air.

The *excretory organs* of the earthworm are *nephridia*, of which there are two in each segment. Each nephridium (Fig. 61) is a long coiled tube opening into the coelom at one end and to the outside at the other end. The funnel-shaped opening from the coelom, and the upper part of the tube, are lined with cilia which maintain a constant flow of liquid (coelomic fluid) down the tube. This liquid contains dissolved waste substances (urea, etc.) which have diffused into the body fluids from the cells, and also solid waste particles derived from the breaking up of blood cells, which act as "scavengers" within the body. The lower part of the tube is composed of gland-cells, and richly supplied with blood capillaries. These gland-cells are generally supposed to absorb waste substances (urea, etc.) from the blood and secrete them into the nephridial tube. By analogy with the action of the kidneys in higher animals (p. 232), however, it seems at least equally probable that these gland-cells absorb water and other useful substances from the liquid (coelomic fluid) in the nephridial tube and secrete them into the blood, the waste substances being automatically eliminated by this selective absorption. The terminal part of the tube is a distensible muscular sac ("bladder") opening to the outside by a minute pore on the ventral surface of the worm.

Vertebrates.—The various groups of higher animals exhibit diverse modifications and complications of the general plan of structure seen in the earthworm. These higher groups do not form a single series of increasing complexity, but rather represent divergent modifications of the coelomate type of structure. We shall consider here only one of these higher groups, the vertebrates. All the largest and most complex animals belong to this group, which includes the fishes, amphibians, reptiles, birds, and mammals. Despite their striking differences in external form, all these animals are very similar in the structure of their nutritive organs. The only important differences among them are in the organs of external respiration and in certain features of the circulatory system closely correlated with these (p. 207).

The general structure of a vertebrate is essentially similar to that of the earthworm (Fig. 62): a tubular enteron, lined with glandular and absorptive endoderm, surrounded by a muscular layer; this is surrounded by a closed body cavity (coelom), enclosed by a thick muscular body wall, covered on the outside by the protective and sensory ectoderm (skin). In the body wall of the vertebrate there is developed an internal *skeleton*, composed of *cartilage* and *bone*, which serves for support of the body, attachment of the muscles, and protection of the internal organs. A vertebrate is also a *segmented* animal, like the earthworm, although in the higher vertebrates there is scarcely any external indication of this segmental structure. The most striking differences in general structure between an earthworm and a vertebrate are due chiefly to the great differentiation, in the latter, among the body segments. A group of segments at the

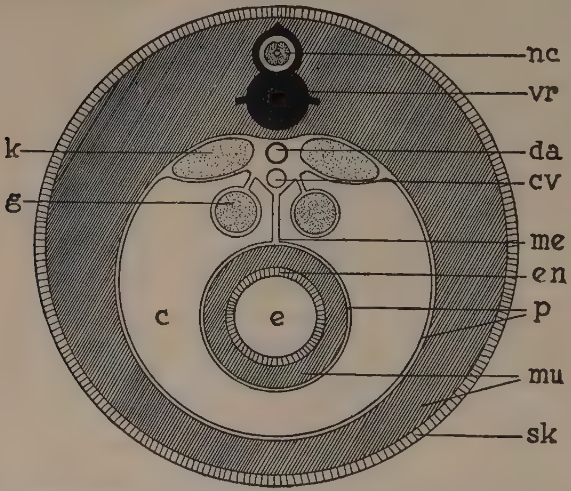


FIG. 62.—Diagrammatic cross-section of a vertebrate. *sk*, skin; *mu*, muscles; *p*, peritoneum; *en*, endoderm; *e*, enteron; *c*, coelom; *me*, mesentery; *k*, kidney; *g*, gonad; *nc*, nerve cord; *vr*, vertebra; *da*, dorsal aorta; *cv*, caval vein.

front end is highly modified to form the *head*, containing the principal part of the nervous system (the brain) and the chief sense organs (eyes, ears, etc.). Other segments are differentiated to form the *limbs*, each of which represents an outgrowth of the body wall of several body segments. In almost all vertebrates there are two pairs of limbs, variously modified, in the different classes, as fins, legs, arms, or wings. The differentiation among the body segments extends also to the internal organs, most of which show little indication of segmental arrangement. In the lower vertebrates (fishes and some amphibia and reptiles), the muscles of the body wall are clearly segmental; but in the higher vertebrates this arrangement of the muscles is highly modified and obscured, and the fundamental segmentation is revealed only by certain parts of the skeleton (backbone and ribs) and of the nervous system (spinal cord).

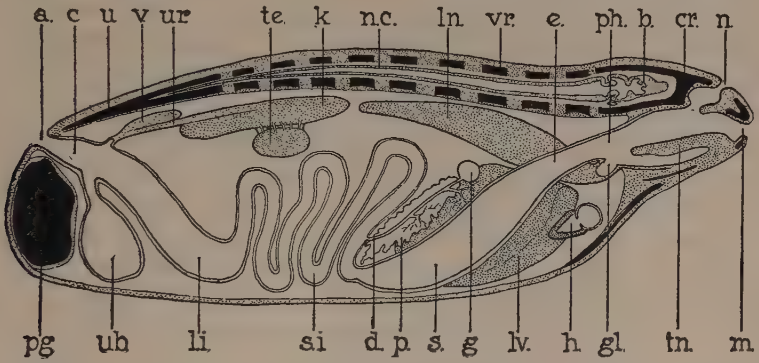


FIG. 63.—Diagrammatic longitudinal section of a frog (male). *n*, nostril; *m*, mouth; *tn*, tongue; *ph*, pharynx; *gl*, glottis; *ln*, lung; *h*, heart; *e*, esophagus; *s*, stomach; *lv*, liver; *g*, gall bladder; *p*, pancreas; *d*, bile duct (with which the ducts from the pancreas unite); *s.i.*, small intestine; *l.i.*, large intestine; *u.b.*, urinary bladder; *c*, cloaca; *a*, anus; *k*, kidney; *te*, testis; *ur*, ureter; *v*, seminal vesicle; *n.c.*, nerve cord (spinal cord); *b*, brain; *cr*, cranium; *vr*, vertebra; *u*, urostyle (terminal portion of vertebral column, made up of several vertebrae fused together); *pg*, pelvic girdle.

The *enteron* is, as in the earthworm, variously modified in different parts of its length into a series of *digestive organs* (Fig. 63). In most vertebrates, the enteron—especially its principal digestive portion, the intestine—is much longer than the body itself, so that it is much twisted and coiled within the body cavity. In the earthworm, the digestive enzymes are produced by single gland-cells (*unicellular glands*) forming part of the general endoderm layer; but in the vertebrates, most of these enzymes are produced by specialized portions of the endoderm constituting *multicellular glands* (p. 274). The smaller of these digestive glands are embedded in the wall of the enteron, but the larger ones (*salivary glands*, *pancreas*, and *liver*) lie in the body cavity entirely outside the enteron, with which they communicate by long *ducts*.

The *circulatory system* consists, as in the earthworm, of a closed system of *blood vessels* containing *blood;* the propulsive power of this system is localized in the *heart*. Side by side with the blood vessels is another set of vessels, the *lymphatic* system, which drains the intercellular spaces, returning their fluid (which is produced continuously by diffusion from the blood capillaries) to the blood.

Almost all vertebrates have special organs of *external respiration*, either *gills* or *lungs;* a few fishes have both, while some amphibia have neither. The skin also plays some part in external respiration, especially in the amphibia.

The chief *excretory organs* are the *kidneys;* these are composed of a large number of tubules, similar in structure and function to the nephridia of the earthworm, but grouped together into a single pair of compact organs instead of being distributed throughout the body.

All these organs are composed of a number of different *tissues*, each consisting of one kind (or at most a few kinds) of cells, connected by more or less intercellular material. The tissues are of two general types: *connective tissues* and *epithelial tissues*. In the connective tissues the cells are irregularly distributed, with a relatively large amount of intercellular material, often much greater in volume than the cells by which it was originally produced; the distinctive characteristics and functions of these tissues are therefore largely determined by the nature of their intercellular materials. This type of tissue is found all through the body, forming the general framework of most organs. Special types of connective tissues are *fat tissue* (p. 214), *cartilage*, *bone*, *ligaments* and *tendons*, *marrow* and *lymphatic tissue*, in which the blood cells are produced, and *blood*, in which the intercellular material is liquid (p. 210). In the epithelial tissues the cells form regular layers and are closely packed, with very little intercellular material. This type of tissue covers all surfaces, both external and internal, forming the outer *skin* and lining the enteron, body cavities, blood and lymph vessels, and all hollow organs. Different types of epithelium differ chiefly in the form and arrangement of their cells: the cells may be flat, cuboidal, or columnar, and may have cilia on the free surface; they may be in a single layer or in several layers. Multicellular *glands* consist of specialized portions of epithelium lining more or less extensive invaginations into which they secrete their products (p. 274). Two very specialized kinds of tissues, *muscular* and *nervous* tissues, though developing from epithelial tissues, are so highly modified that they are generally regarded as distinct types; these will be described in later chapters (Part III). Many of these types of tissues are found in multicellular animals generally.

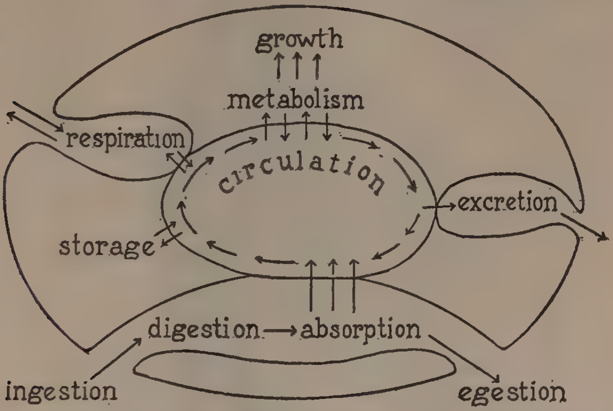


FIG. 64.—Diagram of the nutritive processes of a higher animal.

Nutrition of vertebrates.—Having learned something of the structure of the special nutritive organs of higher animals, we may now consider in more detail the processes of nutrition in a complex multicellular animal. For the sake of brevity and definiteness, we shall confine our attention chiefly to one animal, man, with incidental references to differences in other vertebrates. As a matter of fact, much of our knowledge of nutrition in man has been gained from studies on other animals, particularly other mammals.

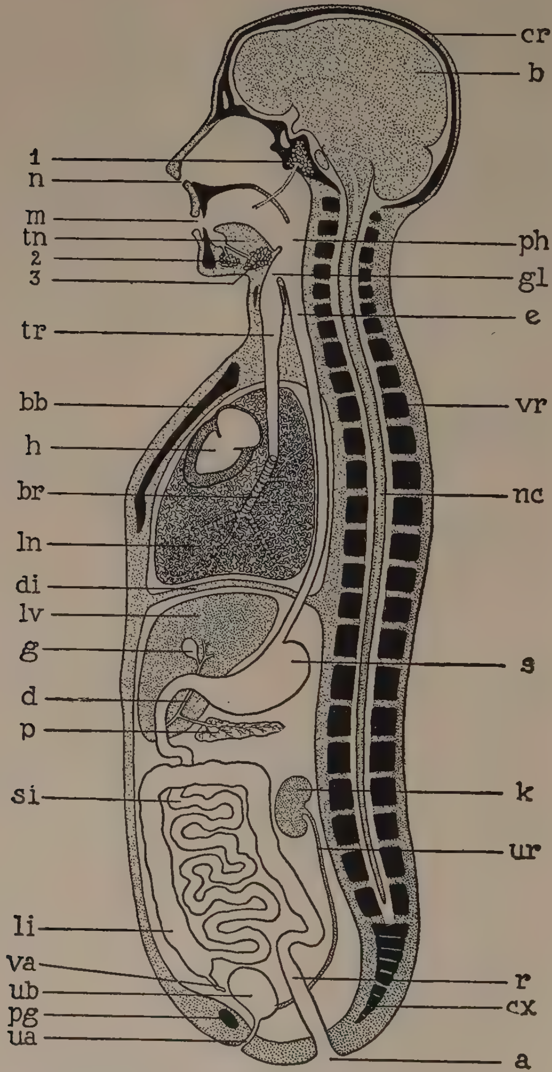

cr
b
1
n
m
tn
2
3
ph
gl
e
tr
bb
vr
h
br
nc
ln
di
lv
g
s
d
p
si
k
ur
li
va
ub
pg
ua
r
cx
a

FIG. 65.—Diagrammatic longitudinal section of man. *n*, nostril; *m*, mouth; *tn*, tongue; *1*, *2*, *3*, salivary glands (*1*, parotid; *2*, sublingual; *3*, submaxillary); *ph*, pharynx; *gl*, glottis; *tr*, trachea; *br*, bronchus; *ln*, lung; *di*, diaphragm; *h*, heart; *e*, esophagus; *s*, stomach; *lv*, liver; *g*, gall bladder; *d*, bile duct; *p*, pancreas; *si*, small intestine; *li*, large intestine; *va*, vermiform appendix; *r*, rectum; *a*, anus; *k*, kidney; *ur*, ureter; *ub*, urinary bladder; *ua*, urethra; *nc*, nerve cord (spinal cord); *b*, brain; *cr*, cranium; *vr*, vertebra; *cx*, coccyx (vestigial tail vertebrae); *bb*, breastbone; *pg*, pelvic girdle.

The interrelations of the various nutritive processes are represented diagrammatically in Fig. 64.

Digestion, in all higher animals, is almost entirely *extracellular*, in the cavity of the enteron. The enteron in man (and in most vertebrates) is differentiated into: *mouth, pharynx, esophagus, stomach, small intestine, large intestine,* and *rectum* (Fig. 65). In the lower vertebrates, the rectum opens into the *cloaca*, which also receives the openings of the excretory and reproductive ducts and opens to the outside through the anus (Fig. 63). In the mammals, however, there is no cloaca, the rectum opening directly to the outside through the anus. The general structure of the wall of the enteron, throughout most of its length, is shown in Fig. 66.

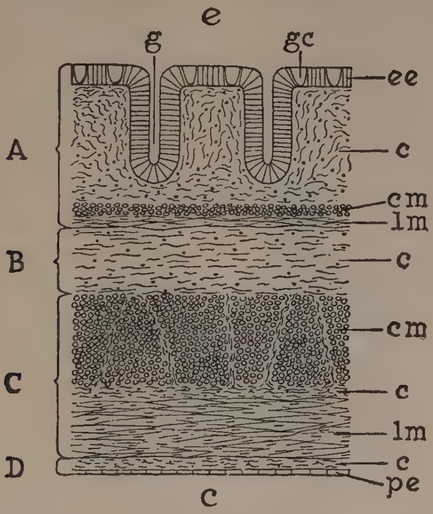


FIG. 66.—Diagrammatic section of a small portion of the wall of the enteron. *A*, mucosa (mucous membrane); *B*, submucosa; *C*, muscular layer; *D*, serosa (serous membrane). *e*, cavity of the enteron; *c* (below), coelom; *ee*, endodermal epithelium; *g*, gland, secreting digestive enzyme; *gc*, goblet cell, secreting mucus; *c*, connective tissue; *cm*, circular muscles; *lm*, longitudinal muscles; *pe*, peritoneal epithelium. The blood vessels and lymphatic vessels, which run chiefly in the connective tissue layers, are not shown in this figure (see Fig. 67).

The *mouth* serves the functions of ingestion, chewing and moistening the food, and, in some animals, partial digestion of starch. In carnivorous animals, the teeth are usually fitted only for seizing and holding the prey, while in herbivorous and omnivorous animals some of them are fitted for chewing. Chewing breaks up the cell walls and the starch grains of plant food, thus facilitating the action of the digestive enzymes. In the mucous membrane of the mouth are many small glands, whose secretion mixes with and moistens the food. This secretion (*mucus*) contains a slimy protein (*mucin*) which lubricates the food, thus facilitating swallowing. In mammals there are also three pairs of larger glands, the *salivary glands*, whose secretion (*saliva*) is discharged into the mouth. In man (and in other omnivorous and herbivorous mammals) the saliva contains an enzyme, *ptyalin*, which catalyzes the hydrolysis of starch. This enzyme has little or no effect on intact starch grains, but attacks rapidly starch which has been cooked or chewed, hydrolyzing it partly to maltose. In carnivorous animals the saliva contains no ptyalin; its chief function is lubrication. These animals do not chew their food, but swallow it whole.

Swallowing is effected by the action of the muscles of the *pharynx*. The passage of the food through the *esophagus* is aided by movements of its muscular wall. These movements are of a type called *peristalsis*, which is characteristic of the muscles of the enteron in all its parts. Peristaltic movement consists of a series of "waves" of contraction and relaxation, travelling always posteriorly; *e.g.*, from the mouth to the stomach. Peristaltic waves are set up in any part of the enteron when it is mechanically stimulated, as by the presence of food inside it.

The *stomach* is a distensible sac with thick muscular walls. In this organ the food is stored temporarily—from one to four hours or longer, depending on the amount and nature of the food—and passed along gradually to the intestine. The food is also largely liquefied (*i.e.*, dissolved or emulsified) and partially digested in the stomach. As it enters the stomach, the food forms a solid ball, which is gradually broken up by the muscular movements of the stomach and the digestive action of its secretions. In the mucous membrane of the stomach are numerous small glands, which secrete a fluid called *gastric juice*. This fluid contains hydrochloric acid to the extent of about 0.4%. Eventually the whole food mass becomes thoroughly disintegrated and acidified. This strong acidity kills many of the bacteria which are always swallowed with the food. The gastric juice also contains an enzyme, *pepsin*, which catalyzes the hydrolysis of proteins. This enzyme acts only in a strongly acid medium, such as exists in the stomach. It can not effect the complete hydrolysis of proteins, to amino-acids, but only their partial hydrolysis, to peptones (p. 55). The posterior end of the stomach is closed by a muscular ring, the *pylorus*. During the first part of digestion in the stomach, the pylorous remains closed, so that food can not escape from the stomach, but is thoroughly churned and mixed with the gastric juice. As the food becomes liquefied and acidified, the pylorus opens at intervals, allowing the stomach contents to escape, a little at a time, into the small intestine. As digestion proceeds the opening of the pylorus becomes more frequent, until finally the whole of the food has passed from the stomach to the intestine.

In the *small intestine*, the food is mixed with three secretions: the *intestinal juice*, produced by small glands in the mucous membrane of the intestine itself; the *bile*, secreted by the *liver;* and the *pancreatic juice*, secreted by the *pancreas*. All these secretions are basic, especially the pancreatic juice, which contains about 0.6% of sodium carbonate; this neutralizes the acidity of the food as it comes from the stomach. None of the enzymes of the pancreatic and intestinal juices can act in a strongly acid medium. The liver and pancreas are large glands whose ducts open into the anterior part of the small intestine. The pancreas is the chief digestive gland in all vertebrates. Its secretion contains three powerful enzymes, *trypsin*, *steapsin*, and *amylopsin*, acting on proteins, fats, and starch respectively. Trypsin acts on both natural proteins and peptones, but more rapidly on the latter. It hydrolyzes them completely, or almost completely, to amino-acids. Steapsin hydrolyzes fats to fatty acids and glycerol. It also liberates fatty acids from other lipins which contain them (*e.g.*, phospholipins). The fatty acids thus liberated are partly converted into soaps (p. 49) by the sodium carbonate of the pancreatic and intestinal juices. These soaps promote the fine emulsification of the remaining fats, which facilitates the action of steapsin on them. Amylopsin acts similarly to ptyalin, hydrolyzing starch to maltose. This is hydrolyzed further, to glucose, by *maltase*, which is present in both the pancreatic and the intestinal juices. The intestinal juice also contains *sucrase* and *lactase*, which hydrolyze sucrose and lactose, respectively, to monosaccharoses (p. 104). Another important enzyme in this secretion is *erepsin*, which acts on peptones, but not on the natural proteins; this enzyme is more effective than trypsin in the very last stages of protein digestion, the liberation of amino-acids. The three enzymes, pepsin, trypsin, and erepsin, acting in this order, effect the complete digestion of proteins more rapidly than any one or any two of them can do alone. The bile contains no important digestive enzymes, but certain of its components, the *bile salts*, play an important rôle in the digestion and absorption of fats. These salts (sodium salts of certain organic acids) aid in the emulsification of fats, enhance the digestive action of steapsin, and dissolve the fatty acids, thus facilitating their absorption. The other components of the bile are chiefly waste substances, excreted in this way; especially the *bile pigments* (p. 210).

The foods, mixed with these digestive juices, are carried along through the small intestine by its peristaltic movements. This is the longest portion of the enteron, about 25 feet long in man. During their passage through it, the food substances are almost completely digested and absorbed. The undigested residues finally escape into the *large intestine*. Here there is no further digestion, except by the action of bacteria, which are always present in enormous numbers in the large intestine. The decomposition of undigested food substances by these bacteria results in the production of various organic acids, amines (organic bases), ammonia, hydrogen sulfide, etc. Some of these substances are very toxic if absorbed. These bacterial actions are favored by any deficiency in the normal digestive processes, or by the indigestible residues remaining in the large intestine too long. In some herbivorous animals, the digestive action of the intestinal bacteria, especially on cellulose, may play an important part in the normal nutrition of the animal.

The principal digestive enzymes in man are summarized in the following table; with a few exceptions (*e.g.*, ptyalin), they are practically the same in all other vertebrates.

Secretion	*Place of Action*	*Enzymes*	*Substrates*	*Products*
saliva	mouth	ptyalin	starch	maltose
gastric juice	stomach	pepsin	proteins	peptones
pancreatic juice	small intestine	trypsin	proteins and peptones	amino-acids
		steapsin	fats (and other lipins)	fatty acids and glycerol
		amylopsin	starch	maltose
intestinal juice	small intestine	maltase	maltose	glucose
		sucrase	sucrose	glucose and fructose
		lactase	lactose	glucose and galactose
		erepsin	peptones	amino-acids

Absorption occurs chiefly in the small intestine. The entire inner surface of the small intestine is studded with minute finger-shaped projections, about 0.5 mm. long, called *villi* (Fig. 67). These increase the total absorptive surface of the intestine about ten times. Each villus consists of a central core of loose connective tissue, containing blood and lymph vessels and a few muscle cells, covered by a single layer of epithelial cells. The products of digestion —glucose, amino-acids, glycerol, fatty acids, etc.—as well as water and soluble inorganic salts, are absorbed by these epithelial cells, from which they pass into the blood and lymph (p. 213). This absorption is a process of osmosis due chiefly to the diffusion of these substances from the region of their greater concentration (the cavity of the intestine) to regions of their lesser concentration (the cells, blood and lymph), according to the law of diffusion. Other physical and chemical factors also enter into the process to some extent (p. 92).

A considerable amount of water is absorbed, along with the dissolved substances, in the small intestine. This amount, however, is scarcely greater than that which is added to the intestinal contents by the various digestive juices. The material reaching the large intestine is therefore still liquid. Most of the remaining water is absorbed in the large intestine. The products of bacterial decompositions may also be absorbed here, sometimes with harmful effects. The remaining solid residues, the *feces*, are egested through the rectum and anus. The feces are composed of indigestible substances taken in with the food, remains of dead intestinal cells and of the various digestive secretions, waste substances excreted in the bile, and large numbers of bacteria, mostly dead. As much as 50% of the feces may consist of dead bacteria. The color of the feces is due chiefly to the bile pigments; their odor to products of bacterial decompositions in the intestine.

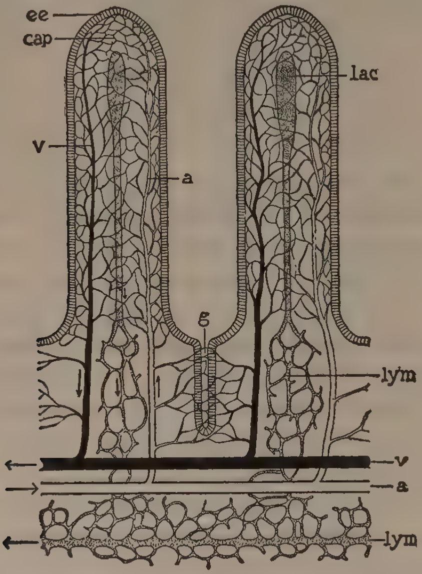


FIG. 67.—Diagrammatic section of two villi, showing their blood vessels and lymphatic vessels. *ee*, endodermal epithelium; *g*, gland; *a*, artery; *cap*, capillaries; *v*, vein; *lym*, lymphatic vessels; *lac*, lacteal, the central lymphatic vessel of the villus. Arrows indicate the direction of flow of the blood and the lymph. The interstices among the blood and lymph vessels are occupied by connective tissue and some muscle cells, not shown in this figure (see Fig. 66).

Circulation of the blood and lymph.—The distribution of the absorbed food substances, as well as the transportation of oxygen, of carbon dioxide and other waste products, and of internal secretions (p. 275) are all effected by the *circulatory system.* The organs of circulation, in vertebrates, consist of two sets of vessels, the *blood vessels* and the *lymphatic vessels*, containing *blood* and *lymph* respectively. The blood vessels constitute, as in the earthworm, a closed system of tubes in which the blood circulates continuously.

They comprise the *heart*, *arteries*, *capillaries*, and *veins*. The circulation of the blood is maintained by the heart, which contracts rhythmically (about 72 times per minute in man). A system of valves in the heart and in the veins keeps the flow always in one direction. The vertebrate heart consists of several chambers—four in mammals (Fig. 68). The *auricles* receive the blood from the largest veins, and force it, by their contractions, into the *ventricles*. The ventricles, which have very thick muscular walls, contract immediately after the auricles, forcing the blood into the largest arteries. The walls of the arteries consist of muscle and elastic connective tissue. They are somewhat distensible, but very elastic. Their elasticity, together with the propulsive force of the heart, maintains the *blood pressure*, which keeps it flowing through the vessels. The largest arteries divide into smaller ones, these into still smaller, and so on. The smallest arteries open into the capillaries, very minute vessels composed of a single layer of flat epithelial cells. The capillaries penetrate the intercellular spaces of all organs and tissues, forming a continuous network throughout the body. Through their very thin walls, osmotic exchanges take place between the blood and the tissues. The capillaries unite to form small veins, which unite to form larger veins, and so on. The veins are relatively thin-walled (as compared with the arteries), very distensible and not elastic. The blood pressure in the veins is very much less than in the arteries, but is sufficient to keep the blood moving in them, back to the heart. The largest veins open into the auricles, thus completing the circulation.

The actual course of the circulation differs somewhat in the different classes of vertebrates (Fig. 68). In the fishes, which breathe by means of *gills* (p. 223), there is only one auricle and one ventricle. From the ventricle, a large artery runs forward, and divides into branches which go to the gills. In each gill, the arteries break up into a network of capillaries, in which the blood is *aerated*, *i.e.*, exchanges CO_2 and oxygen with the surrounding water. These gill capillaries reunite to form arteries (not veins), which unite to form a large artery on the dorsal side. From this, branches are given off to all parts of the body. Thence the blood passes into the capillaries, to the veins, and so back

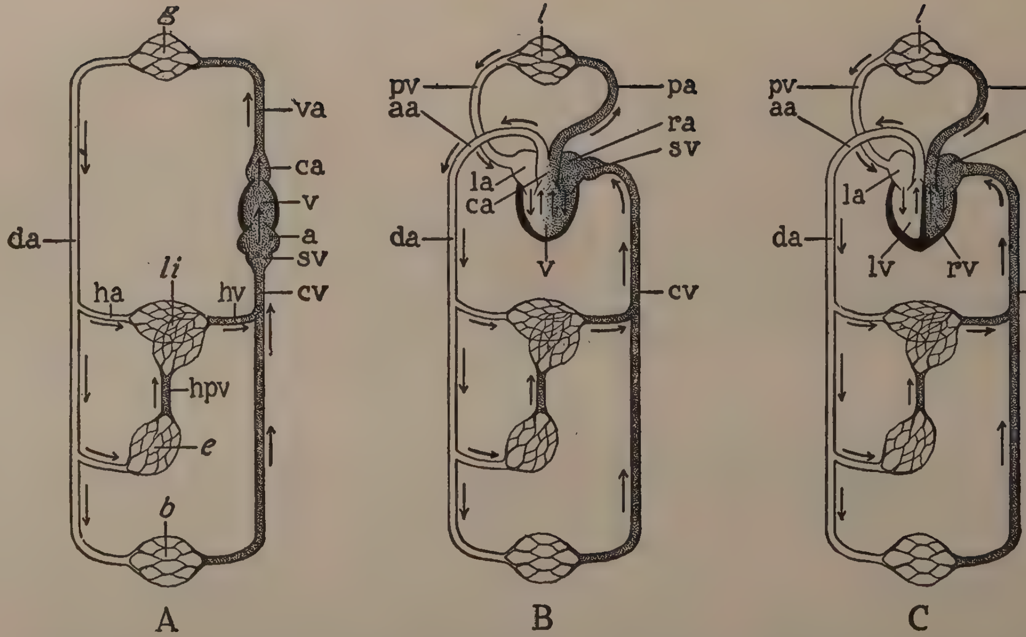

g
va
ca
v
a
sv
cv
da
li
ha
hv
hpv
e
b
A
l
pv
aa
pa
ra
sv
la
ca
da
v
cv
B
l
pv
aa
pa
ra
la
da
lv
rv
cv
C

FIG. 68.—Diagrams of the circulation of the blood in (*A*) fish, (*B*) frog, (*C*) mammal. Arrows indicate the direction of flow of the blood; the shading represents unaerated blood, the unshaded portions aerated blood. *a*, auricle; *la*, left auricle; *ra*, right auricle; *v*, ventricle; *lv*, left ventricle; *rv*, right ventricle; *ca*, conus arteriosus; *va*, ventral aorta; *da*, dorsal aorta; *aa*, aortic arch; *pa*, pulmonary artery; *pv*, pulmonary vein; *ha*, hepatic artery; *hpv*, portal vein; *hv*, hepatic vein; *cv*, caval vein (vena cava); *sv*, sinus venosus; *g*, capillaries of the gills; *l*, capillaries of the lungs; *e*, capillaries of the enteron; *li*, capillaries of the liver; *b*, capillaries of the rest of the body.

to the heart. This type of circulation is called a *single circulation.* In the amphibia and reptiles, breathing by means of *lungs* (p. 224), there are two auricles and one ventricle. The main artery opening from the ventricle gives off branches, the *pulmonary arteries*, to the two lungs, and other branches to the rest of the body. The pulmonary arteries form capillaries in the lungs, which reunite to form the *pulmonary veins.* The pulmonary veins open into the *left auricle*, while all the other veins open into the *right auricle.* Thus the left auricle receives aerated blood from the lungs, while the right auricle receives unaerated blood from the rest of the body; these are, however, more or less mixed in the ventricle, into which both auricles open. This type of circulation is called an *incomplete double circulation.* In the warm-blooded animals—birds and mammals—there are two auricles and two ventricles. Only the pulmonary arteries open from the *right ventricle;* the pulmonary veins return aerated blood to the left auricle: this is called the *pulmonary circulation.* The left auricle opens into the *left ventricle*, which pumps blood into a large artery giving branches to all other parts of the body; thence the unaerated blood returns to the right auricle: this is called the *systemic circulation.* The right auricle opens into the right ventricle, thus completing the circulation: right auricle → right ventricle → pulmonary circulation → left auricle → left ventricle → systemic circulation → right auricle. There is no direct communication between the right and left sides of the heart, so that the aerated and unaerated blood are kept entirely separate. This type of circulation is called a *complete double circulation.*

One very important feature of the circulation, common to all vertebrates, is the *hepatic portal system.* The veins from the digestive organs (stomach, intestine, etc.) join to form the large *portal vein*, which does not return direct to the heart, but goes to the *liver*, where it breaks up into capillaries again. The liver is a very large organ and has an unusually rich supply of capillaries, so that it contains more blood than any other organ of the body. Part of this is aerated blood, brought by the *hepatic artery;* but most of it is blood brought by the portal vein, containing the digested food substances absorbed from the intestine. From the capillaries of the liver the blood passes into the *hepatic vein*, which returns it to the heart.

The *blood*, contained within the blood vessels, is a fluid tissue, consisting of a liquid intercellular material, the *blood plasma*, and several kinds of cells, the *blood corpuscles* (Fig. 69). The blood cells are of two main kinds: *red blood corpuscles* and *white blood corpuscles*. An adult man contains about 5 liters of blood, constituting about one-thirteenth of the entire body weight. The plasma and the corpuscles each constitute about one-half of the whole blood. The red corpuscles number about 5,000,000 per cubic millimeter of blood; *i.e.*, about 25×10^{12} in the whole human body. The white corpuscles number about 10,000 per cubic millimeter, or 5×10^{10} in the whole body; but their number is very variable. The red corpuscles of mammals are thin, biconcave disks, about 8.5 μ in diameter, without nuclei; *i.e.*, they are cells which have lost their nuclei. In the lower vertebrates, they are larger, elliptical, nucleated cells. They contain a large proportion (about 30%) of *hemoglobin*, which plays an essential rôle in respiration (p. 226). It is this substance which gives the red color to the corpuscles and to the whole blood, the plasma being colorless. The red corpuscles are produced in the *marrow* of the bones. Their average length of life, after losing their nuclei and being set free in the blood, is about 10 days. They are destroyed in the liver, which excretes the products of decomposition of hemoglobin as the bile pigments (p. 204). The iron, however, is mostly retained in the body and used over again in the synthesis of hemoglobin. Red blood corpuscles are found only in vertebrates; hemoglobin when present in invertebrates (*e.g.*, the earthworm) is dissolved in the plasma. The white blood cells, or *leucocytes*, are motile,

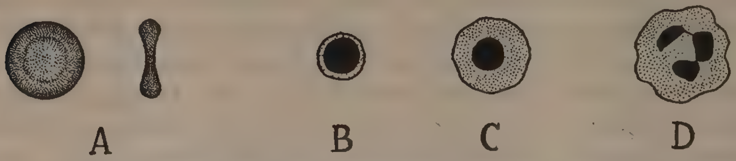


FIG. 69.—Red and white blood corpuscles of man, all drawn to the same scale. *A*, red blood corpuscle, flat and edgewise; *B*, lymphocyte; *C*, mononuclear leucocyte; *D*, polymorphonuclear leucocyte.

amoeboid cells, of several different types, from 5 μ to 10 μ in diameter. They crawl about, like amoebae, not only within the blood vessels, but through all the cavities and intercellular spaces of the body. They get out of the blood vessels by squeezing out between the epithelial cells of the capillaries. Like amoebae, they can ingest solid particles. In this way, they aid in the transportation of insoluble food substances (*e.g.*, fats); in the removal of waste materials, especially the remains of dead cells; and in the destruction of bacteria which have got into the body. Leucocytes, or "wandering cells," are found in all multicellular animals, even those which have no blood system. In vertebrates, the leucocytes are produced in the bone marrow and also in the *lymphatic tissues* which occur in many organs of the body. The blood plasma is a dilute solution of proteins, salts, food and waste substances; its average composition is approximately:

	Per Cent
Water	92
Proteins	6.5
Lipins	0.5
Inorganic salts	0.8
Glucose	0.1
Amino-acids	0.05
Urea and other waste substances	0.05

Practically every substance found in any part of the body is present in the blood, in greater or less amount, on its way to or from the various organs. But the blood proteins, and to some extent its salts, are peculiar to the blood. The blood proteins are supposed to be produced, in part at least, by the leucocytes. One of these proteins, *fibrinogen*, is of special interest in connection with the *clotting* of the blood in wounds. This phenomenon is due to a series of reactions among certain components of the blood and of the wounded cells, whereby the soluble fibrinogen is converted into a much less soluble protein, *fibrin*. The latter forms a gel, entraining the plasma and corpuscles in its meshes; this forms the blood clot, which stops further bleeding. The chief salt in the blood plasma is *sodium chloride*, which is much less abundant in the cells. Another important salt in the plasma is *sodium bicarbonate*, which plays an essential rôle in respiration (p. 227).

The blood pressure within the vessels continuously forces a certain amount of plasma through the very thin walls of the capillaries into the intercellular spaces. This fluid is called the *lymph.* It has practically the same composition as the blood plasma, but with a somewhat smaller proportion of proteins. It also contains leucocytes, which escape from the blood vessels as previously described. Lymph is therefore practically blood without any red corpuscles; it is a colorless fluid. The lymph is a kind of "middleman," through which osmotic exchanges of dissolved food and waste substances are effected between the blood and the cells.

Since the lymph is being continuously produced by filtration from the blood capillaries, it must be as continuously removed from the intercellular spaces. This is effected by a system of vessels called *lymphatic vessels.* These have the same structure and distribution as the capillaries and veins of the blood system. They ramify through all the organs of the body alongside the blood vessels. The flow of lymph through these vessels is maintained by the blood pressure which produces it. In some of the lower vertebrates (*e.g.*, frogs) there are also small pulsating organs, called *lymph hearts*, in the course of some of the larger lymphatics, which help to propel the lymph. The large lymphatic vessels have valves which permit its flow in only one direction. The largest lymphatic vessels finally open into some of the large veins of the blood system, thus returning the lymph to the blood. In the mammals, most of the lymphatics open into one large vessel, the *thoracic duct*, which empties into one of the large veins near the heart. In the course of many of the lymphatic vessels occur *lymph nodes*, composed of lymphatic tissue, which produce some of the leucocytes.

The circulatory system, comprising the blood and lymph and their vessels, is the vehicle of transportation of all substances within the body. Its functions include: *distribution* of food substances absorbed from the intestine to all parts of the body; transportation of oxygen and carbon dioxide in *respiration;* transportation of other waste products of metabolism for *excretion;* transportation of internal secretions for *coordination* of the activities of various organs (p. 321); and *protection* of the organism against internal parasites, such as bacteria.

Distribution of absorbed food substances.—The mucous membrane of the intestine is richly supplied with both blood and lymph vessels. Each villus (Fig. 67) has a small artery bringing blood to a network of capillaries immediately under the absorptive epithelium, and a small vein carrying this blood away to the portal vein. In the center of each villus is a club-shaped lymphatic vessel, ending blind near the free end of the villus, and communicating, beneath the villi, with a network of lymphatic vessels which lead eventually to the thoracic duct. The interstices of the loose connective tissue framework of the villus contain lymph and many leucocytes. Each villus also has a few muscle cells, extending lengthwise through it, by means of which it can contract.

Most of the digested food substances absorbed from the intestine—glucose, amino-acids, etc.—diffuse from the absorptive epithelial cells into the blood capillaries immediately beneath them. From these they are carried by the blood, through the portal vein, *to the liver*. From the liver they are carried by way of the hepatic vein to the heart and thus into the general circulation. From the blood capillaries, in every part of the body, the food substances diffuse into the lymph in the intercellular spaces, and thence into the cells, where they are metabolized.

The products of fat digestion, absorbed chiefly as glycerol and fatty acids (or soaps), are, to a large extent, resynthesized into true fats in the epithelial cells of the villi. This fat, in the form of small drops, is extruded by the epithelial cells into the interior of the villus. Here part of it is ingested by the leucocytes, which crawl into the central lymphatic vessel and there disintegrate, liberating the fat droplets in the lymph. Other fat droplets pass from the epithelial cells into the lymphatic vessel without the aid of leucocytes, probably assisted by contractions of the muscle cells of the villus. This fat-laden lymph is carried through the lymphatic vessels to the thoracic duct and thence into the blood, thus getting into the general circulation without passing through the liver. Part of the products of fat digestion may pass, in soluble forms (glycerol, soaps, phospholipins, etc.), from the intestinal epithelium into the blood capillaries, like the other food substances. The total amount of lipins in the blood may be increased to double its normal quantity after digestion and absorption of a fatty meal; this excess disappears from the blood within a few hours, most of it being taken up by the *fat tissues*, in various parts of the body, where it is *stored*, chiefly as true fats, in the form of large fat globules within the cells.

Metabolism in the liver.—Most of the food substances absorbed from the intestine are carried, by way of the portal vein, to the liver. This organ is a great "chemical factory" which transforms the food substances in various ways, stores some of them temporarily, and regulates the amounts of the different kinds of food substances in the blood and thus their supply to the other tissues.

Carbohydrates are absorbed as monosaccharoses, chiefly glucose. In the liver, the other monosaccharoses (fructose, galactose, etc.) are converted into glucose, and most of the glucose is synthesized into glycogen, which is *stored* in the liver cells. The interconversion of glucose and glycogen is, as we have previously seen (p. 116), a reversible reaction. When glucose is being absorbed from the intestine, after digestion, it reaches a relatively high concentration in the portal blood, from which it is absorbed by the liver cells. The reaction glucose $\rightleftharpoons$ glycogen then goes in the synthetic direction; *i.e.*, most of the glucose is converted into glycogen. Between meals, or during starvation, when the concentration of glucose in the blood tends to fall, it diffuses out of the liver cells, and the reaction then goes in the opposite direction; *i.e.*, glycogen is hydrolyzed to glucose. These processes serve to maintain a normal concentration of glucose in the blood, about 0.1%, which remains fairly constant, even in starvation. The liver thus serves as a storehouse of reserve carbohydrate food, upon which the other organs (muscles, etc.) can draw at need, through the blood stream. Glycogen is formed and stored in other cells, especially muscle cells, also, but to a much smaller extent: the liver of a well-fed animal may contain as much as 15–20% of glycogen, whereas other organs seldom contain more than 1–3%.

Proteins are absorbed from the intestine as *amino-acids*. The first step in the destructive metabolism of amino-acids, *deamination*, is performed chiefly, though not entirely, in the liver. Their amino radicals are split off as *ammonia*, which is then converted into *urea* (p. 115). Ammonia produced by deamination in other organs is absorbed from the blood by the liver cells, and also converted into urea. The liver is thus the chief seat of urea production in the vertebrate body. This urea passes out into the blood, from which it is eventually removed by the kidneys (p. 231). In reptiles and birds, most of the urea is converted, also in the liver, into a somewhat more complex nitrogen compound, *uric acid*, which is the chief nitrogenous excretion of these animals. A small amount of uric acid is produced by the liver in some mammals (*e.g.*, man) also, but this is produced by oxidation of certain organic bases (derived chiefly from the destructive metabolism of nucleic acid).

The non-nitrogenous residues of the amino-acids may be oxidized in the liver cells, may be carried by the blood to other cells where they are oxidized, or may be converted into glucose and glycogen (p. 116). Protein foods may thus serve as a source of stored glycogen in the liver and of glucose supply to the cells. Not all the amino-acids of the food are deaminized in the liver; a small amount must be used in constructive metabolism (p. 220), and some are deaminized in other cells. When the diet contains a large proportion of proteins, however, the greater part is metabolized in this way in the liver. After a meal rich in proteins, most of their nitrogen is excreted, as urea, within a few hours. In carnivorous animals, whose food consists largely of proteins, most of the protein is probably converted into carbohydrate in this way.

The liver cells also absorb from the portal blood many of the toxic substances produced by bacterial action in the intestine, and convert them into non-toxic compounds. The *bile salts* (p. 204), which are re-absorbed from the intestine unchanged, are also absorbed by the liver cells from the blood and re-secreted in the bile. Thus there is a regular "circulation" of the bile salts: from the liver, in the bile, to the intestine; from the intestine, in the blood of the portal vein, back to the liver.

Fats, as we have seen, do not go directly to the liver from the intestine, but they reach it eventually, of course, through the general circulation, and the liver plays a rôle in the metabolism of these substances also. The fats of the food, and those stored in the fat tissues, consist largely of *saturated* fatty acids, having the general constitution $C_nH_{2n}O_2$ (p. 49). These acids are not easily fragmented and oxidized in the cells. In the liver, these acids are partly *desaturated; i.e.*, some of the hydrogen is removed from them. The resulting *unsaturated* fatty acids are more readily metabolized in the other tissues. Simple fats may also be converted, in part, to phospholipins in the liver. Fat may also be *stored* in the liver, but usually not to any great extent.

Besides these special metabolic processes which occur chiefly in the liver, its cells perform also the general metabolic processes common to all living cells. Because most of the blood supply of the liver is unaerated blood (brought by the portal vein), the oxygen supply to the liver is relatively small: oxidation processes are therefore less, in proportion to its size, than in other organs; *i.e.*, the metabolism of the liver is, to a certain extent, anaerobic. Most of the metabolic processes of the liver, described above, occur also in other cells; but in cells with a better oxygen supply these intermediate metabolic products are immediately oxidized. In the liver, however, they escape oxidation, and are carried by the blood to other organs. The special metabolism of the liver is therefore partly due to its deficient oxygen supply. To some extent, also, it is due to special enzymes in the liver cells, which are absent or less abundant in other cells.

General metabolism.—The processes of ingestion, digestion, and absorption, and the reversible storage processes of the liver and fat tissues serve to maintain in the blood fairly constant amounts of glucose, amino-acids, fats, etc. From this constant food supply, the living cells of the body draw the substances used in the metabolic processes which maintain their life. The greatest part of the total metabolism of a higher animal is that of the muscles, since these constitute the largest part of the living cells of the body. The metabolism of other tissues (nerve tissue, glands, etc.) is essentially similar to that of the muscles, and may be even greater in proportion to their size, but the total amount of food consumed by them is only a small fraction of the total metabolism of the body.

The chemical reactions of metabolism in the animal cell have been discussed previously (Chapter VII). We shall discuss here some quantitative aspects of the requirements and utilization of food in the higher animals, especially man.

In contrast to plants (p. 180), animals use by far the greater part of their food in *destructive metabolism*, to supply the energy expended in the physical activities of the animal. Many very accurate experiments have shown that under all conditions the energy expended, as work and heat, by a man or other animal is exactly equal to the chemical potential energy of the food substances oxidized in the body during the same period. This is the proof of the exact applicability of the law of Conservation of Energy to the living organism (p. 13), and also proves that the sole source of the energy expended in the activities of an animal is the chemical potential energy of its food.

The amount of energy expended by any individual animal depends on its size, its body temperature, its degree of activity, etc. As an example, the following table shows, roughly, the amount of energy expended by an average (150 lb.) man per day, under various conditions.

Conditions of activity	*Energy expended*
Complete rest, fasting	1600 Calories per day
Complete rest, eating	1800 Calories per day
Indoor life, no work	2200 Calories per day
Sedentary work	2400 Calories per day
Manual labor	3000 Calories per day

The minimum energy expenditure of 1600 calories represents the heat required to maintain the body temperature (37° C), and the continuously essential work of internal organs, *e.g.*, heart, lungs, etc. The next 200 calories represents the work of eating and of the digestive organs, and the increased rate of metabolic reactions due to the greater concentrations of food substances in the cells (p. 96). The subsequent increments represent the energy expended, as mechanical energy and heat, by the activity of the muscles of arms, legs, trunk, etc.

In "warm-blooded" animals (birds and mammals) only a small proportion—on the average about 5%—of this energy leaves the body as mechanical energy, the rest being liberated as heat and expended to maintain the *body* *temperature.* In these animals the temperature of the body is practically constant, irrespective of the temperature of their surroundings. The body temperatures of most mammals and birds are between 35° and 40° C (in man, 37° C). The surrounding air is usually considerably cooler: seldom over 20°–25° C, and often much colder. These animals are therefore constantly dissipating heat to their surroundings; this heat can be produced only by the oxidation of organic food substances in the body. In "cold-blooded" animals, whose temperature is always practically the same as that of their surroundings, there is less heat production, and therefore a smaller amount of food consumed in oxidation. Even in these animals, however, the quantity of food consumed in destructive metabolism is probably always much greater than that used for constructive metabolism.

The energy thus expended by the animal is supplied by oxidation, in its cells, of metabolic fragments derived chiefly from carbohydrates, fats, and the non-nitrogenous residues of amino-acids after deamination (p. 114). The total energy liberated by a series of chemical reactions depends, as pointed out previously, only on the nature of the initial substances and the final products, regardless of the intermediate steps. The energy liberated by the principal classes of organic food substances, as they are oxidized in the animal body (*i.e.*, carbohydrates and fats completely oxidized, to CO_2 and H_2O; proteins incompletely oxidized, to CO_2, H_2O, and urea), is approximately:

Carbohydrates	4 Calories per gram
Fats	9 Calories per gram
Proteins	4 Calories per gram

So far as energy supply is concerned, these three classes of food substances are interchangeable in the proportions indicated by these figures; *e.g.*, an energy expenditure of 2400 Calories could be balanced by the consumption of 600 grams of carbohydrate, or 600 grams of protein, or 100 grams of fat plus 375 grams of carbohydrate, etc. In fact, as we have seen (p. 116), these substances are largely interconvertible in the animal cell.

When the food eaten is more than sufficient to balance the current energy expenditure, the excess may be *stored* as glycogen or fat. *Glycogen* is synthesized from glucose—or, indirectly, from other substances (p. 215)—and stored, not only in the liver but also, to a smaller extent, in all cells. This store of glycogen within the cell serves as an immediately available source of glucose. During rapid energy-releasing metabolism (*e.g.*, muscular contraction, glandular secretion, etc.), the glycogen breaks down into glucose, which is fragmented and oxidized (p. 113). In the intervening periods of relative inactivity, the glycogen reserve of the cell is replenished by absorption of glucose from the blood. *Fat* is the most abundant form of stored food in the animal body. It may come directly from the fats of the food or may be synthesized in the cells from carbohydrate (p. 116). Fat is the most "economical" form of food storage: because of its greater potential energy per gram and its insolubility in water, it permits the storage of a greater amount of potential energy in the same space than any other food substance. Most of the reserve fat is stored in the special fat tissues, a smaller amount in the muscles and sometimes in the liver; other organs normally contain practically no true fats.

In starvation—that is, when the total food supply from outside is inadequate—the organism consumes first its store of glycogen. After this is exhausted, the stored fats are next the chief source of energy. When these have been used up, the organism begins to consume itself, *i.e.*, the organic components of its protoplasm, chiefly proteins and phospholipins. When this self-consumption has been continued long enough to seriously affect the essential organs, death ensues. Only a very small proportion of the proteins and phospholipins of such organs as the brain, heart, and kidneys is consumed before the fatal termination of starvation.

In an adult animal in which the body as a whole is not increasing in weight, only a very small proportion of the food intake is used for constructive metabolism. Thus, in an average adult man, whose total consumption of organic food substances is about 600–700 grams per day, not more than 15–20 grams of this (chiefly protein) is used in constructive metabolism; *i.e.*, not more than 2.5–3% of the total. This small amount is used for the formation and growth of new cells to replace those which are constantly dying (*e.g.*, blood corpuscles, outer layers of the skin, etc.), for the synthesis of digestive enzymes and other secretions necessary to the life processes, etc.—or, as it is often put, in general terms, to replace the "wear and tear" of the tissues incidental to their normal functioning. When the body is gaining weight, the amount of food constructively metabolized—either assimilated as protein, etc., or stored as fat—is, of course, somewhat greater. In an infant at the age of most rapid growth (the first few months after birth), the amount of organic food substances used for constructive metabolism—growth—may be as high as 15% of the total intake. All the rest is oxidized to yield energy. This is in striking contrast to plants, which expend much less energy in physical activity and therefore use a much larger proportion of their food substances for constructive metabolism (p. 180).

The amount of protein food required to maintain the body at constant weight is somewhat greater than the minimum amount actually used in constructive metabolism. Thus, although the amount of protein thus used by an adult man may be not more than 15 grams per day, it is found that about 50 grams per day is necessary to prevent loss of body weight. This is because a certain proportion of the amino-acids derived from the proteins of the food is always destroyed by deamination (chiefly in the liver) before they have a chance to be re-synthesized into proteins in the cells. It seems that not more than about one-third of the total amino-acids of the food proteins can actually become available for constructive metabolism. If this is insufficient to balance the loss of proteins, in the various ways mentioned above, the organism must lose weight. Any excess of protein in the food, above the actual daily requirement, is deaminized, its nitrogen excreted as urea, and the remainder oxidized just like carbohydrate. There is no storage of "inert" protein—comparable to the storage of glycogen and fat—in the animal body. If the protein in the food is insufficient to meet the daily requirements of metabolism, part of the living protoplasm of the cells must be sacrificed to meet the deficiency. Some amino-acids can be synthesized in the animal from carbohydrate and ammonia (p. 116). But as proteins are normally the only source of ammonia in the animal body, these syntheses can only help to conserve the protein supply by using the ammonia over again instead of excreting it; they cannot make good an actual deficiency of protein (*i.e.*, of organic nitrogen compounds) in the food. Many of the amino-acids, especially those of more complex structure, cannot be synthesized at all in the animal body, but must be supplied "ready made" in the proteins of the food. Thus the food must contain not only an adequate total amount of protein, but also the necessary minimum amount of every amino-acid which cannot be synthesized in the organism. The nutritive "efficiency" of any particular kind of food protein depends on the kinds and proportions of different amino-acids it contains. It can seldom happen that the proteins of the food are "100% efficient" in this sense; *i.e.*, that they contain all the different amino-acids in exactly the proportions required by the body to replace its "wear and tear." This is another reason why the actual protein requirement is greater than the theoretically necessary minimum.

Water is produced by the oxidations of organic food substances in the cells (p. 113). In land animals, however, the amount of water thus produced is much less than the amount continually lost from the body, chiefly through the lungs and kidneys. In a man, for instance, the amount of water produced by oxidation in the body is not more than 300–400 grams per day, while the amount lost from the body is at least 3000 grams daily. Water must therefore be taken in as a food, to maintain the normal amount in the body. Most food materials, of plant or animal origin, contain considerable proportions of water, usually enough to supply most of the amount required; this may be supplemented by drinking water.

Inorganic salts are not "used up" in metabolism as the organic food substances are. When the body weight is stationary, the amounts of these salts in the body remain practically constant. There is, however, a constant "leakage" of salts from the body, chiefly through the kidneys (p. 231). To balance this loss, the salts which are essential components of protoplasm or of the blood, bones, secretions, etc., must be taken in as foods. The minimum daily intake of the principal elementary constituents required to maintain salt "balance" in an adult man is approximately:

Phosphorus	1.	gram per day
Chlorine	1.	gram per day
Potassium	1.4	gram per day
Sodium	0.9	gram per day
Calcium	0.5	gram per day
Magnesium	0.2	gram per day
Iron	0.01	gram per day

Part of the phosphorus and iron are supplied by proteins (p. 54); the other elements listed are taken in almost entirely as inorganic salts. There are also a few other elements (*e.g.*, iodine, fluorine, silicon) essential to the human organism in very minute quantities, which are also obtained in the form of inorganic salts. Most of these salts are contained, in usually adequate amounts, in the food materials of plant or animal origin; small quantities are also contained in drinking water. Animals which live largely on plant food need to eat sodium chloride, because these two elements are absent, or nearly so, in most plants (p. 39).

It has been discovered in recent years that there are required, by man and some other animals, very small quantities of certain organic substances whose chemical constitution is still unknown: these are called *vitamins* or *accessory food substances.* At least four or five different vitamins (called vitamin A, vitamin B, etc.) are definitely known to be essential food substances of man and some other mammals and some birds; the nutrition of other animals has been very little studied in this respect. The amounts required are not definitely known, but they are very minute; somewhat larger quantities are required for growth than for maintenance of the adult animal. The chemical constitution of none of these substances is yet completely known; they are all organic substances, some are lipins (*i.e.*, fat-soluble), others are water-soluble, probably nitrogenous, substances. They are contained, in usually adequate amounts, in many food materials of plant or animal origin; they are undoubtedly, like other organic compounds, synthesized by plants from inorganic substances. Their uses in the organism are still unknown; presumably they form, or contribute to the formation of, some substances with catalytic or "regulative" functions. The lack, or inadequate supply, of any particular vitamin in the diet of an animal is manifested by definite abnormalities, called "deficiency diseases," which may be fatal if the diet is not corrected. They are apparently "used up" in some way in the animal, as a continued supply is necessary, although they can be stored up in the body to some extent. While the nature and functions of vitamins are important scientific problems, their practical dietary importance has been greatly exaggerated, as there is little chance, in the ordinary diets of civilized man, of a diet adequate in other respects being deficient in any necessary vitamin.

Respiration.—In vertebrates, as in the earthworm and many other animals, the exchange of oxygen and carbon dioxide between the cells and the external environment is effected by way of the blood. The processes involved in respiration therefore include: the aeration of the blood (*external respiration*); the transportation of O_2 and CO_2 by the blood between the organs of external respiration and the rest of the body; and the exchange of these gases between the blood and the cells (*internal respiration*).

Almost all vertebrates have special organs for aeration of the blood. In fishes these are the *gills;* in land vertebrates, the *lungs.* Both these kinds of organs are developed from the enteron in the region of the pharynx. Gills (Fig. 70) develop as a series of openings in the sides of the pharynx, extending out through the body wall as the *gill slits.* The partitions between these slits are the *gill arches.* The mucous membrane covering the gill arches is produced into a large number of long thin filaments, the *gill filaments;* these are the actual organs of respiration. A current of water flows in through the mouth to the pharynx and out through the gill slits, bathing the gill filaments. Each filament contains a network of blood capillaries lying close under its surface epithelium. The blood in these capillaries is separated from the outside water only by the very thin wall of the capillary and the epithelium of the gill filament. Through this membrane, CO_2 diffuses outward and O_2 inward, because of the differences in the concentrations of these two gases in the blood and the water (p. 120). This constitutes the "aeration" of the blood.

Lungs (Figs. 63, 65) develop as a hollow outgrowth from the ventral wall of the pharynx, which grows backward in the body cavity and branches to form the two lungs. In the lower air-breathing vertebrates (*e.g.*, frogs), the lungs are simple elastic sacs, opening anteriorly into a common chamber, the *larynx*, which communicates with the pharynx by a narrow slit, the *glottis*. On the inner surface of each lung there is a complex network of ridges abundantly supplied with blood capillaries, in which the aeration of the blood takes place. In the mammals, the structure of the lungs and the air passages leading to them is more complex. From the larynx a wide tube, the *trachea*, runs backward through the neck into the chest, where it divides into two branches, the *bronchi*, one leading to each lung. Within the lungs, the bronchi divide and subdivide to form a ramifying system of smaller and smaller tubes. The terminal branches, or *bronchioles*, open into minute air sacs, the *alveoli* (Fig. 71). The walls of the alveoli are composed of very thin flat epithelial cells. Although each alveolus is very small (diameter about 0.2 mm.) the number of alveoli in the lungs is enormous, so that their total surface is very large. The number of alveoli in the human lungs is probably over a billion, and their total surface about 200 square meters; only about two-thirds of these, however, are ordinarily filled with air. All through the lungs there is a fine network

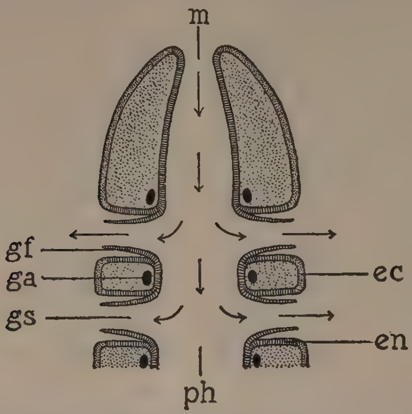


Fig. 70.—Diagram of the gills of a fish (shark). Arrows indicate the direction of flow of water. *m*, mouth; *ph*, pharynx; *gs*, gill slit; *ga*, gill arch; *gf*, gill filament; *ec*, ectoderm; *en*, endoderm.

of blood capillaries, in immediate contact with the alveolar epithelium. The blood in these capillaries is separated from the air in the alveoli only by the very thin epithelial cells of the capillary and the alveolar walls, whose aggregate thickness is only about 4 μ. By diffusion through this very thin membrane, the exchange of O_2 and CO_2 between the air and the blood is effected.

Since the lungs are blind sacs, there is no "circulation" of air through them; the air in them can be renewed only by alternately emptying and filling them. This is accomplished by the respiratory movements, or *breathing*. The mechanism of breathing is very different in the various groups of air-breathing vertebrates. In the mammals, it is effected by movements of the *ribs* and of the *diaphragm*, a transverse muscular partition dividing the body cavity into an anterior part, the *thorax*, which contains the lungs, and a posterior part, the *abdomen* (Fig. 65). In *inspiration*, the ribs move upward and outward and the diaphragm downward, enlarging the cavity of the thorax; thus air is sucked into the lungs. In *expiration*, the diaphragm and the muscles of the ribs simply relax; the elasticity of the lungs then expels the air. In ordinary breathing only about one-sixth of the air in the lungs is inspired and expired at each breath. The alveolar air is thus merely diluted with fresh air, so that it always contains less O_2 and more CO_2 than the outside atmosphere. The average proportions of these two gases are:

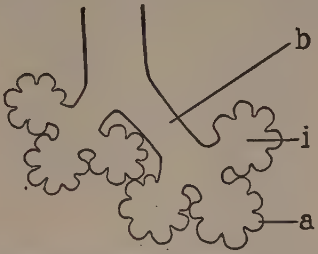


FIG. 71.—Diagram of the structure of a small portion of the human lung. *b*, bronchiole; *i*, infundibulum; *a*, alveolus.

	O_2 *Per Cent*	CO_2 *Per Cent*
in atmospheric air	21	0.03
in alveolar air	13	5

The walls of the alveoli are always moist, since water is constantly diffusing out of the blood and the cells. In this film of moisture, the gases of the alveolar air dissolve. The amount of oxygen dissolved in this film, under the conditions (of concentration, pressure, and temperature) in the lungs, is greater than the concentration of free oxygen in the unaerated blood brought to the lungs by the pulmonary arteries. Oxygen therefore diffuses through the alveolar and capillary walls into the blood. On the other hand, the concentration of CO_2 dissolved in the lungs is less than that in the unaerated blood; it therefore diffuses from the blood into the alveoli. The blood thus gains O_2 and loses CO_2 in passing through the capillaries of the lungs. This aerated blood is carried by the pulmonary veins back to the heart and thence to the systemic circulation (Fig. 68). The amount of oxygen consumed by a man under average conditions is about 400 cc. per minute; the amount of carbon dioxide produced about 350 cc. per minute.

The amounts of oxygen and carbon dioxide transported by the blood are much greater than could be simply dissolved in the water of the blood. The amounts of these gases which would dissolve in water under the conditions (of concentration, pressure, and temperature) in the body, compared with the amounts actually carried by the blood, are:

		O_2	CO_2
		Per Cent	*Per Cent*
solubility in water		0.3	3
amount in blood	aerated	20	40
	unaerated	12	45

It is evident, therefore, that the greater part of both these gases in the blood is not simply dissolved, but must be chemically combined with some components of the blood. Practically all the oxygen in the blood (except the very small amount in solution) is combined with *hemoglobin* in the red corpuscles. This substance combines with oxygen, in the proportion of one molecule of hemoglobin to one molecule of oxygen, forming *oxyhemoglobin:*

$$\text{hemoglobin} + O_2 \rightleftharpoons \text{oxyhemoglobin}$$

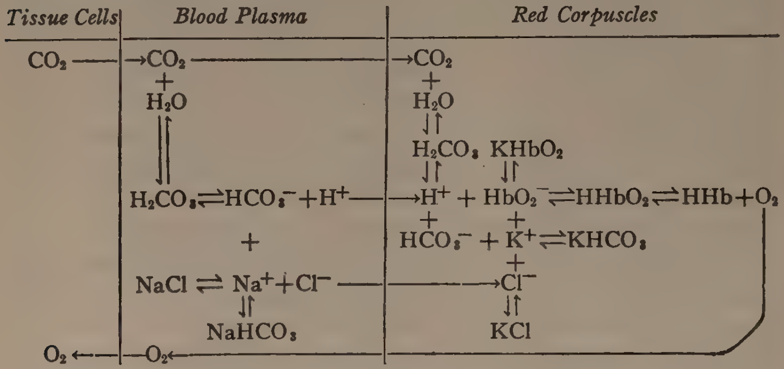
This reaction is reversible and, like all reversible reactions, goes in either direction according to the relative concentrations of the reacting substances (p. 96). Thus in the capillaries of the lungs, where oxygen is relatively abundant, the hemoglobin is converted almost entirely (about 95%) into oxyhemoglobin. In the capillaries of the other organs, where the concentration of oxygen is much lower, the reaction goes in the opposite direction: oxyhemoglobin is reduced to hemoglobin, liberating O_2. Under average conditions, however, only about 40% of the oxyhemoglobin is thus reduced; *i.e.*, unaerated blood contains about 60% as much oxygen as aerated blood. The difference in color between aerated ("arterial") and unaerated ("venous") blood is due to the different proportions of oxyhemoglobin and hemoglobin: the former is a brighter red.

Carbon dioxide is also carried by the blood in chemical combination, mostly as *bicarbonates*. About two-thirds of the total carbon dioxide of the blood is in the plasma, chiefly as sodium bicarbonate, $NaHCO_3$; the other third in the corpuscles, chiefly as potassium bicarbonate, $KHCO_3$. The chemical changes which take place when CO_2 is added to the blood, in the capillaries of the systemic circulation, are very complex. The principal ones are those involving hemoglobin. It will be recalled that proteins can combine with either acids or bases; *i.e.*, they act as bases in acidic solutions, and as acids in basic (and usually also in neutral) solutions (p. 52). The blood is an almost neutral (very slightly basic) solution. Under this condition, both hemoglobin and oxyhemoglobin act as acids, but oxyhemoglobin is more strongly acidic than hemoglobin. The oxyhemoglobin therefore exists, to a greater extent than the hemoglobin, as anions, associated with inorganic cations, chiefly K^+. As CO_2 enters the blood and O_2 leaves it, in the systemic capillaries, the following reactions occur simultaneously:

$$CO_2 + H_2O \rightarrow H_2CO_3 \rightarrow H^+ + HCO_3^-$$

$$\text{oxyhemoglobin} \rightarrow \text{hemoglobin} + O_2$$

Each of these reactions aids the other: the increased acidity due to CO_2 accelerates the decomposition of oxyhemoglobin; and this acidity, in turn, is neutralized by the change of oxyhemoglobin to the weaker acid hemoglobin. The principal reactions involved may be represented in the following schematic form (HHb and $HHbO_2$ represent un-ionized hemoglobin and oxyhemoglobin respectively, and HbO_2^- oxyhemoglobin anions):



These reactions show how carbon dioxide is carried as $NaHCO_3$ in the blood plasma and $KHCO_3$ in the corpuscles (the plasma membrane of the corpuscles is impermeable to Na^+ and K^+ ions); and also how the blood can absorb large quantities of CO_2 with very little increase in acidity. Since all these reactions are reversible, there are always small amounts of uncombined O_2 and CO_2 in simple solution in the blood. It is the concentrations of these dissolved gases which determines, directly, their diffusion between the blood and the tissue cells, on the one hand, and between the blood and the alveoli of the lungs on the other hand. In the capillaries of the lungs, all these reactions go in the opposite direction. The oxidation of hemoglobin to oxyhemoglobin, a stronger acid, helps to break up the bicarbonates and drive CO_2 out of the blood into the alveoli; the escape of CO_2, in turn, by decreasing the acidity of the blood, accelerates the oxidation of hemoglobin. Either O_2 or CO_2 added to the blood would tend to make it acid; but as one of these gases is always leaving when the other is entering the blood, their effects largely balance each other. Thus the blood normally always remains almost exactly neutral (very slightly basic); if the blood actually becomes even very slightly acidic, the animal dies.

In all the living cells of the body, oxygen is being continually used up, and carbon dioxide produced, by the oxidative metabolism of the cells. Consequently the concentration of O_2 in the cells is always close to zero, while the concentration of CO_2 is greater than that in the blood. The O_2 liberated from oxyhemoglobin therefore diffuses from the blood, via the lymph, into the tissue cells; and CO_2 diffuses in the opposite direction. This constitutes *internal respiration*, *i.e.*, the respiration of the cells.

Excretion.—The waste products of metabolism of the cells of the animal body are carbon dioxide, water, inorganic salts (chiefly phosphates and sulphates derived from oxidation of proteins), urea and other nitrogenous compounds (ammonia, uric acid, etc.), and many other simple organic compounds in very small amounts. All these waste products, as well as toxic or useless substances which may be absorbed with the foods, must be eliminated from the body. Carbon dioxide is eliminated almost entirely through the lungs; water is also eliminated largely through the lungs, by evaporation. Most of the other waste substances are excreted by the *kidneys*, the chief excretory organs of vertebrates (Fig. 72). These are a pair of organs in the dorsal part of the body cavity. Each kidney is composed of a large number of long convoluted *urinary tubules* (Fig. 73),

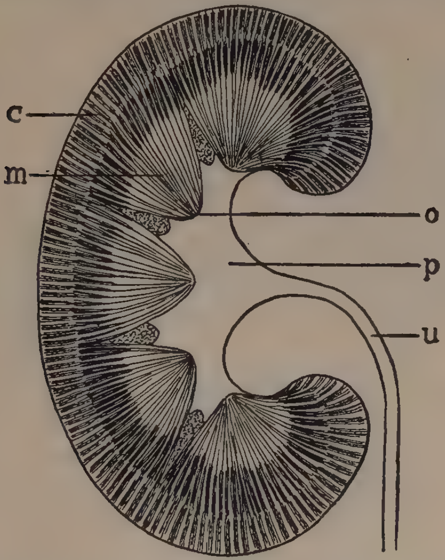


FIG. 72.—Longitudinal section of human kidney. *c*, cortex (consisting chiefly of glomeruli and urinary tubules); *m*, medulla (consisting chiefly of collecting tubules); *o*, point where collecting tubules open; *p*, pelvis; *u*, ureter.

somewhat similar in structure and function to the nephridia of the earthworm. In many of the lower vertebrates, these tubules open into the coelom by ciliated funnels, as in the earthworm; but in the higher vertebrates they do not. Each tubule begins in a spherical, double-walled *capsule*, surrounding a bunch of blood capillaries, the *glomerulus*. The walls of the capsule are composed of very thin, flat epithelial cells, in close contact with the blood capillaries of the glomerulus. The remainder of the tubule—the long, convoluted portion—is composed mostly of columnar epithelium, like that of absorptive and glandular tissues, and surrounded by a network of blood capillaries. The connections of the blood vessels are such that the blood flows first through the glomeruli and thence through the capillaries surrounding the tubules. All the tubules of each kidney open into a single chamber, the *pelvis*, from which runs a duct, the *ureter*. In lower vertebrates the two ureters open into the cloaca (Fig. 63); but in mammals they open directly into the *bladder*, which opens to the exterior by a single duct, the *urethra* (Fig. 65).

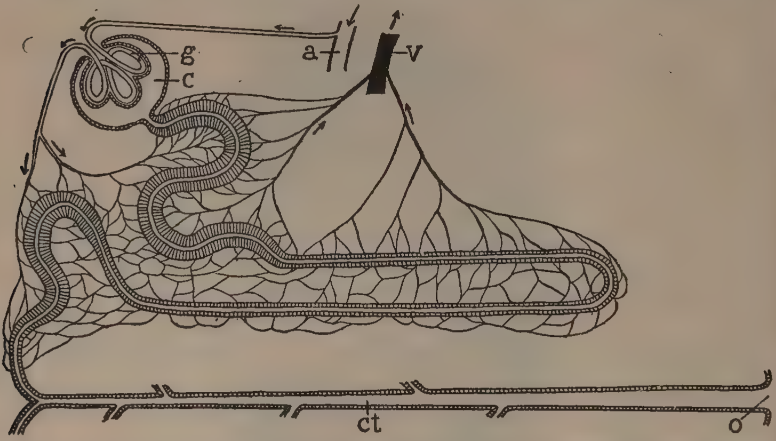


FIG. 73.—Diagram of a urinary tubule, with its blood vessels. Arrows indicate the direction of flow of the blood. *a*, artery; *v*, vein; *g*, glomerulus; *c*, capsule; *ct*, collecting tubule, into which a number of urinary tubules open; *o*, opening of collecting tubule to pelvis of the kidney.

The fluid excreted by the kidneys, the *urine*, is composed entirely of substances present in the blood plasma; the kidney does not produce the substances it excretes, but merely separates them from the blood. The urine contains, in fact, all the diffusible (crystalloidal) components of the blood plasma, but in very different proportions. The average composition of human urine, compared with that of blood plasma, is approximately:

	Urine	*Blood plasma*	*Ratio* $\frac{\textit{urine}}{\textit{plasma}}$
	%	%	
Urea	2	0.033	60
Other N compounds (uric acid, ammonia, etc.)	0.3	0.01	30
Sulphate	0.18	0.003	60
Phosphate	0.18	0.009	20
Sodium chloride	1.	0.65	1.5
Other salts (K, Ca, Mg, etc.)	0.3	0.14	2
Glucose	trace	0.1	less than 1
Amino-acids	trace	0.05	less than 1
Total crystalloids	4	1	4
Colloids (proteins and lipins)	0	7	
Water	96	92	

Thus we see that the urine, compared with the blood plasma from which it is formed, contains none of its colloids; only traces of the organic food substances such as glucose and amino-acids; a slightly larger proportion of most inorganic salts; and a much greater proportion of waste products such as urea and sulphate. Substances such as phosphates, which figure in metabolism as both food and waste substances, occupy an intermediate position.

The work of the kidney is therefore the partial separation of the components of the blood circulating through it: holding back, within the body, the useful substances, and excreting the waste products. This work is done by the urinary tubules, of which there are about 16,000 in each kidney. There are two distinct processes involved: one in the glomerulus, the other in the tubule itself. In the glomerulus, the blood is simply *filtered* into the cavity of the tubule. The thin walls of the glomerular capillaries and the capsule surrounding them act as a "colloidal filter," which is impermeable to the blood colloids (and, of course, to the corpuscles) but permeable to water and all the crystalloids of the plasma. The fluid in the upper end of the urinary tubule is therefore simply blood plasma minus its colloids (proteins and lipins). It contains all the components of urine, but in different proportions. The composition of this solution must evidently be changed, quantitatively, to produce the urine. This change is effected, chiefly at least, by *reabsorption* of some of the water and dissolved substances from the cavity of the tubule by the epithelial cells forming the greater part of the tubule. The extent of this reabsorption differs greatly in the different groups of vertebrates. In some marine fishes, there may be little or no reabsorption (except, perhaps, of some of the organic food substances); the process of excretion is little more than simple filtration, and the urine is practically colloid-free blood plasma. In fresh-water amphibia, such as frogs, a large part of the salts (*e.g.*, sodium chloride), as well as organic food substances (glucose, etc.), are reabsorbed in the urinary tubules, so that the urine is *hypotonic* (p. 82) to the blood plasma. These animals, living in fresh water, are continually absorbing water by osmosis through the skin; their kidneys serve, like the contractile vacuoles of fresh-water protozoa (p. 120), to eliminate this excess water. The frog therefore excretes a large volume—more than its own body weight per day—of very dilute urine, consisting chiefly of water. If the ureters of one of these animals be tied, so as to prevent excretion of urine, the animal will actually swell up enormously, because of the absorption of water through the skin. In the higher land vertebrates (reptiles, birds, and mammals), the situation in respect to water is just the opposite. These animals are constantly losing water, by evaporation, more rapidly than it is produced in the body by oxidation. This evaporation is prevented, to some extent, by protective skin coverings—scales, feathers, or hair—but the loss of water, especially through the lungs, is still more rapid than its production in the cells. To these animals, therefore, water is primarily a food substance rather than a waste substance. In these classes of vertebrates, a large proportion of water is reabsorbed in the urinary tubules, producing urine which is *hypertonic* to the blood plasma. In reptiles and birds, in fact, this process goes even further: more water is reabsorbed from the urine in the cloaca, so that the urine as voided is semisolid in consistency, like the feces. The quantitative composition of the urine as it leaves the kidneys, in the higher vertebrates (*e.g.*, man), may be explained by the reabsorption in the urinary tubules, from the glomerular filtrate, of a solution of definite constant composition, which may be called "normal colloid-free blood plasma." The result of this process is the excretion of everything not reabsorbed; *i.e.*, waste products, foreign substances, and any other substances present in amounts above their normal concentrations in the plasma. The composition of the urine therefore varies according to the diet and other factors affecting the actual composition of the blood plasma from time to time. The constant reabsorption by the tubule cells of water, salts, etc., in their normal proportions—regardless of their actual concentrations, at the moment, in the plasma and therefore in the glomerular filtrate—results in maintaining an extremely constant composition of the blood. The function of the kidneys, in the higher vertebrates, may therefore be said to be primarily the *regulation of the composition of the blood.*

The *work* (energy expenditure) of filtering the blood plasma in the glomerulus is done, not by the kidney itself, but by the blood pressure; *i.e.*, in the final analysis, by the heart, which produces the blood pressure. Additional work must be done, however, to concentrate this dilute filtrate to the composition of the urine. The urine (as shown by the figures given above) contains about four times as much of solutes as the colloid-free plasma, and therefore has an osmotic pressure about four times as great (p. 81). This means that, in the urinary tubules, water must be absorbed from a *hypertonic* solution; *i.e.*, *against* the force of osmosis (p. 78). To absorb water against osmotic force requires the expenditure of energy, just as it does to lift a weight against gravitational force. This energy is produced in the absorptive cells of the urinary tubules by the oxidation of food substances. If these cells be killed, or their oxygen supply cut off, the urine has the composition of colloid-free blood plasma; *i.e.*, the process of reabsorption is stopped. How the chemical energy of oxidation is transformed, in the cells, into *osmotic work*—a form of molecular energy—is, as yet, unknown (p. 92).

In addition to the processes of filtration and reabsorption, it is believed by some that the cells of the urinary tubules absorb waste substances (urea, sulphate, etc.) *from* the blood and excrete them *into* the cavity of the tubule. The evidence for this is not conclusive, and some of the leading students of the subject believe that all the facts of urine production can be explained by filtration in the glomeruli and reabsorption in the tubules.

The kidneys are not the sole, though by far the most important, path of excretion in vertebrates. Small amounts of waste substances are excreted by the *sweat glands* of the skin in mammals. Certain waste substances, especially the bile pigments, are excreted by the *liver* in the bile (p. 204). The secretions of the intestinal glands and other digestive glands also contain some waste substances, which are eliminated through the intestine. The feces, however, can not be regarded primarily as excretions, since they consist mostly of matter which has never been in the cells of the organism, but only within the cavity of the enteron (p. 206).

Summary of nutritive mechanisms of animals.—

	Protozoa	*Hydra*	*Planaria*	*Earthworm*	*Vertebrates*
Ingestion	pseudopodia or "mouth"	mouth (and pseudopodia of endoderm cells)	mouth	mouth	mouth
Digestion	food vacuoles	partly in cavity of enteron; chiefly in endoderm cells	chiefly in cavity of enteron; partly in endoderm cells	cavity of enteron	cavity of enteron
Egestion	surface of cell	mouth	mouth	anus	anus
Absorption	by protoplasm from food vacuoles	by endoderm cells from enteron and food vacuoles	by endoderm cells from enteron	by endoderm cells from enteron	by endoderm cells from enteron
Distribution	intracellular diffusion	diffusion from cell to cell	intercellular fluid	blood and intercellular fluid	blood and lymph
Metabolism	in protoplasm of every living cell				
Respiration	surface of cell	surfaces of all cells	ectoderm and intercellular spaces	skin and blood	lungs or gills, and blood
Excretion	surface of cell; contractile vacuole	surfaces of all cells	flame-cells and excretory tubules	nephridia	kidneys

CHAPTER XIII

STIMULATION AND RESPONSE

THE activities of organisms are, in general, not continuous and uniform, but ever changing, in kind and extent, in response to changes in the surroundings or inside the organism itself. This property of *responsiveness*—changes in behavior determined by changes in conditions—is by no means peculiar to living things, but is common to all material systems. The more complex the composition and structure of the system, the more complex and varied are its responses.

One very characteristic feature of many, though not all, responses of organisms is that the magnitude of the response is out of all proportion to that of its apparent cause. A very slight stimulus—touch, sound, light, etc.—may occasion very extensive and energetic responses. This is also true of many non-living systems. This kind of effect may be called "trigger action," by analogy with the action of a trigger which sets off an explosion, starts an engine, or releases a weight. In all such cases the effect is a sudden liberation of energy which has been contained in the system in some potential form. In the organism this is the chemical potential energy of food substances in the cells, which is transformed into kinetic energy by chemical reactions of the "downhill" type—decompositions, oxidations, etc. As pointed out previously (p. 14), the form in which this kinetic energy is manifested, in each particular case, depends on the structure of the machine in which the transformation occurs. From this point of view, a living organism is a machine for the transformation of chemical potential energy into various forms of kinetic energy, which constitute the activities of the organism. The only distinctive characteristic we can ascribe to the responses of living, as compared with non-living, things is their greater complexity: because the machine is more complex, chemically and physically, it is capable of responding to a greater variety of conditions and of responding in more complex and varied ways.

Stimulus and response.—Every activity, or change in activity, of an organism may be regarded as a *response* to some *stimulus*. The stimulus may be some physical or chemical change in the external environment, or it may be internal, *i.e.*, some preceding change inside the organism itself. A response of one part of the organism to some previous stimulus may, in turn, stimulate some other part, and so on. Thus the activities of the organism are continually modified by its own previous activities as well as by external events. Each response may also bring the organism into a different relation to its surroundings, resulting in a new stimulus. In this way, a constant external condition—light, gravity, etc.—may apparently act as a continual stimulus. In the broadest sense, then, we may define a stimulus as any *change in relation* between an organism and its surroundings—whether due to external events or the organism's own activities—or between different parts of the organism, which modifies the activities of the organism in any way.

To avoid confusion in the use of the terms stimulus and response, we must distinguish carefully between what may be called the "continuous" and the "explosive" types of response. A very gradual change of some condition—*e.g.*, pressure, temperature, or concentration of some substance—may effect an equally gradual change in the rate or character of metabolism, in the form or structure of the cell, etc.; a change which is directly related and more or less proportional to the external change determining it. Such continuous changes in the activities of a cell are responses, in the broadest sense of the word, and the conditions responsible for them may be regarded as stimuli. What we usually mean, however, when speaking of responses and their stimuli, are changes of the "explosive" type, in which the stimulus acts as a "trigger" to release suddenly a store of energy in the cells. To act in this way, the stimulus must itself be a relatively quick, though it may be a very slight, change of some external or internal condition. This type of response shows no special relation, qualitatively or quantitatively, to the stimulus arousing it, but depends, rather, on the structure and internal conditions of the cell itself, *i.e.*, on its energy content and the "machinery" through which this is discharged. In the following pages, the words stimulus and response will be used in this sense.

Excitation.—Every response of the "explosive" type is accompanied, or preceded, by a momentary altered state of the cell, called the *state of excitation*, of which the most striking indication is an electrical discharge, the *action current*. This phenomenon is shown by every kind of cell when effectively stimulated. In the resting—*i.e.*, unexcited—state, the plasma membrane of the living cell is electrically *polarized:* that is, it has opposite electric charges on its inner and outer surfaces. This is probably due to the plasma membrane being, in its normal state, impermeable to some of the negative ions inside the cell, while it is permeable to the positive ions associated with them. These positive ions, however, can not escape very far from the outer surface of the cell, because they are held back by the electrostatic attraction of the indiffusible negative ions (p. 71). This results in the formation of an *electrical double layer:* positive ions outside the membrane, negative ions inside (Fig. 74). There is thus an electrical potential difference (*i.e.*, a difference of charge) between the outside and the inside of the cell. When any two points of different electrical potential are connected by a conductor (*e.g.*, a metal wire), an electric current flows from the region of

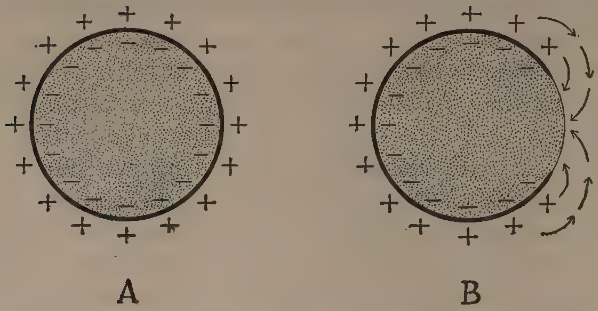


FIG. 74.—Diagram illustrating the theory of excitation. *A*, cell in the normal, unexcited state: the cell membrane is electrically polarized, as indicated by the signs. *B*, the cell excited at one point; the permeability of the cell membrane is increased, and its polarization abolished, at the point of excitation; arrows indicate direction of the action current.

greater positive (or smaller negative) charge to that of smaller positive (or greater negative) charge.[1] If two points on the outer surface of a normal, unexcited, cell or tissue—*e.g.*, a muscle—be so connected, no current will flow, since all such points are positively and equally charged. But if the tissue be cut at one point, a current will flow through a conductor from the normal (positively charged) to the cut (uncharged) surface. The same effect is obtained if the cells are injured in any way at one point: this increases the permeability and therefore abolishes the polarization of the plasma membrane at the injured point. A similar condition is produced, momentarily, when a cell is excited by a stimulus; there is an increase in permeability of the membrane at the point of excitation, which abolishes its polarization by allowing the free movement of ions in both directions. / This results in a potential difference between the neighboring unexcited cell surfaces, which are positively charged, and the excited region, which is now uncharged. A momentary current will therefore flow—through a connecting wire, or through the electrolytic solutions normally surrounding the cells—from the unexcited to the excited cells or parts of a cell: this is the *action current*, which always accompanies and is the best indication of the state of excitation. These bio-electric currents—the injury currents and action currents—can be readily detected and measured by means of a sensitive electrical measuring instrument (a galvanometer or an electrometer): their electromotive force (voltage) is usually between 0.01 and 0.1 volt. These electric currents, produced by the cells themselves, are capable of stimulating neighboring cells. In this way the state of excitation is transmitted from one cell, or part of a cell, to another; this is the mechanism by which a stimulus at one point may produce responses in other parts of the organism.

The increased permeability of cells when stimulated, which gives rise to the action current, is shown also in other ways: by the entrance or escape of dissolved substances to which the plasma membrane is ordinarily impermeable.

---

[1] The "direction" of flow of an electric current is purely a matter of convention; *by definition*, the direction of flow is from the region of positive to the region of negative potential, without reference to the actual direction of movement of the ions or electrons which carry the electricity.

This increase of permeability is presumably due to some change in the protoplasmic structure (p. 89). This change is not necessarily confined to the plasma membrane, or surface layer of the protoplasm; it may extend more or less throughout the protoplasm of the cell. If this increased permeability, or the structural change underlying it, is essential to the state of excitation, we should expect that any substance or condition which tends to increase the permeability of the cell would also increase its *irritability* (susceptibility to stimulation); while anything which decreases its permeability should make the cell more resistant to stimulation. This is, in fact, true: sodium and potassium salts, for instance, increase both permeability and irritability; while calcium and magnesium salts, and also many organic compounds, have the opposite effects (p. 86). Any substance which increases the irritability of cells may be called a *stimulant;* substances which decrease irritability are called *narcotics* or *anaesthetics*. Some substances (*e.g.*, alcohol, ether, etc.) may act first as stimulants; in greater concentrations, or acting for a longer time, they act as narcotics; in still greater concentrations they are toxic, killing or permanently injuring the cells (p. 87).

The state of excitation involves also some chemical change, which may be the immediate cause of the structural change. This chemical reaction must be of the "downhill" type, since it liberates a small amount of energy in the form of heat as well as that of the action current, but it does not consume oxygen; *i.e.*, it is some kind of decomposition not involving oxidation, such as the fragmentation of carbohydrate to lactic acid (p. 113). The excitatory state is always followed, however, by more extensive and prolonged chemical reactions which consume oxygen and produce carbon dioxide and a larger amount of heat, involving the oxidation of some food substances or intermediate products of metabolism within the cell. These oxidation processes are associated with the restoration of the cell to its original, unexcited, state; *i.e.*, they supply energy for the rebuilding of the normal protoplasmic structure.

Immediately after excitation, before the cell has completely returned to its normal state, there is a brief *refractory period*, during which it can not be excited again by any stimulus however strong. The duration of this refractory period varies, in different kinds of cells, from 0.001 second or even less (in nerve cells) to several seconds or minutes (in plant cells). The state of excitation is thus automatically self-limiting: a cell can not remain continuously in a state of excitation. The rhythmic activity of certain organs, such as the heart, is due to this refractory period after each response, during which the cells are incapable of excitation. Many other activities which appear to be continuous—*e.g.*, the prolonged contraction of a skeletal muscle—are actually very rapid rhythmic responses.

In some cases, the effect of a stimulus is the cessation of some activity of the cell. This effect, which is called *inhibition*, may be interpreted as a prolonged refractory period, during which the cell is incapable of normal excitation.

Kinds of stimuli.—Many kinds of physical or chemical changes are capable of acting as stimuli. These may be classified according to the form of energy involved as:

Mechanical stimuli: contact, pressure, sound
Thermal stimuli: changes of temperature
Osmotic stimuli: changes of osmotic pressure
Chemical stimuli: changes in concentration of particular substances
Electrical stimuli: changes in strength or direction of electric currents
Photic stimuli: changes in intensity, color, or direction of light

The effectiveness as stimuli of any of these changes depends not only on the nature and extent of the change, but also on its *rate; i.e.*, the change must have a certain degree of "suddenness" in order to arouse excitation. Different kinds of cells differ greatly in their sensitiveness to these kinds of stimuli. Thus, all cells are susceptible to electrical stimuli, but the amount and rate of change of current strength necessary to stimulate depends on the kind of cell and its condition at the moment. On the other hand, only certain kinds of cells are susceptible at all to photic stimuli. The susceptibility of any particular cell to stimulation depends not only on the nature (composition and structure) of the cell, but also on its condition at the time, as affected by previous excitation, nutrition, oxygen supply, action of various salts and other chemical substances (stimulants or narcotics), etc.

Kinds of responses.—The nature and magnitude of the response also depend on the nature and condition of the cells stimulated. Some kinds of cells (*e.g.*, sensory cells, nerve cells) give no externally perceptible response except the action current, which may stimulate other neighboring cells. Many types of cells, however, show, in addition to and usually following the electrical response, special types of response which depend on the specialized structure or metabolic processes of these cells. Some of these special responses are:

Mechanical response: movement, of the whole organism or some part of it, effected by a sudden change of shape or size of cells; *e.g.*, contraction (shortening) of muscle cells, amoeboid movement, ciliary movements, turgor movements (in plants), etc.

Secretion: a sudden release from the cell of substances previously synthesized and stored within it.

Luminescence: the production of light (*e.g.*, by fireflies).

Color changes: usually effected by contraction or expansion of special pigment cells, *chromatophores* (*e.g.*, in the skin of many fishes, frogs, lizards, etc.).

Electric discharges of considerable strength (200–400 volts): action currents greatly intensified by the special structure and arrangement of the cells composing the *electric organs* (in a few kinds of fishes).

The nature of the response depends only on the kind of cell stimulated, not on the nature of the stimulus. Thus, a muscle cell responds to any kind of effective stimulus—electrical, mechanical, chemical, etc.—by contracting; a gland cell by secreting; a nerve cell by transmitting a state of excitation (the *nerve-impulse*), which is exactly the same regardless of the kind of stimulus arousing it. The magnitude of the response of the cell is also independent of the strength of the stimulus, provided this be sufficient to stimulate the cell at all. The magnitude of the response of a multicellular organ—*e.g.*, the strength of contraction of a muscle—depends on the number of cells stimulated, as well as on the condition of these cells immediately before and during the response. But the response can not be increased by increasing the strength of the stimulus beyond what is just sufficient to stimulate all the cells. Any one cell responds, to any stimulus which excites it at all, with the maximum response of which it is capable at the time: this is called the *all-or-none law.*

Receptors, conductors, and effectors.—The visible response to a stimulus often occurs in some part of the organism other than that originally stimulated. We may distinguish three steps involved in such a response: the *reception* of the stimulus at its point of incidence; the *conduction* of excitation to other parts of the organism; and the *effective* response, which produces some externally perceptible effect. This chain of events is, in reality, a series of responses to stimuli, each of the cells involved being stimulated in turn by the electrical response (action current) of the cells previously stimulated. The whole system may be compared to a train of gunpowder with a match at one end and a barrel of powder at the other: the combustion of the match, which may be started by a very slight stimulus, initiates an explosive reaction which is transmitted by the powder train to the barrel, where it produces an "effective" explosion. The processes in the organism are very similar in principle, though the form of energy involved in the transmission is electrical instead of thermal; in both cases, it should be noted, the source of this energy, at each point in the chain, is the chemical potential energy of the system.

In many organisms, especially the higher animals, there are particular cells or organs specialized for these functions. *Receptors* are cells or organs which are specially fitted, by their position and their special susceptibility to some one kind of stimulus (*e.g.*, light, contact, etc.), for the reception of stimuli, especially those of external origin. *Conductors* are cells or organs specialized, by their form, arrangement, and special susceptibility to electrical stimuli (action currents), for the conduction of excitation within the organism. *Effectors* are cells or organs of special response (movement, secretion, etc.). In the higher animals, such as man, these three kinds of mechanisms are represented by the sense organs, the nerves, and the muscles and glands, respectively. In many unicellular organisms, we find parts of the single cell specially differentiated for reception, conduction, or movement.

Receptors, conductors, and effectors, together, may be called the *responsive mechanisms* of organisms.

Responsive mechanisms of unicellular organisms.—Amoeba is susceptible to external stimuli (contact, etc.), and capable of movement and secretion. Its visible response—*e.g.*, formation of a pseudopodium—may be at a different point than the stimulus, so that its protoplasm must also be capable of conduction. There is no evidence in this organism of any structures specially differentiated for these functions: all parts of the cell seem to be equally capable of reception, conduction, movement and secretion. In many other unicellular organisms, however, there are visibly differentiated structures which serve as receptors, conductors, or effectors.

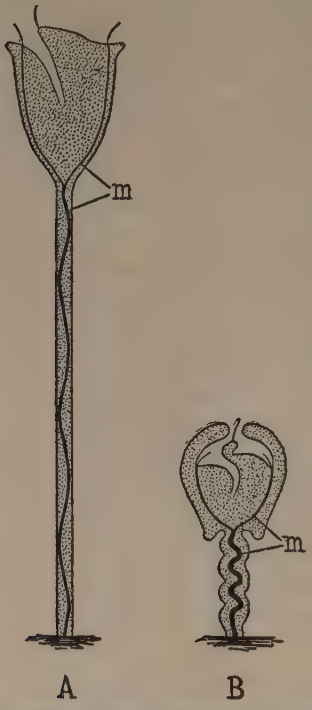


FIG. 75.—Vorticella, a stalked ciliate protozoan: *A*, expanded; *B*, contracted. The contraction is effected by the shortening of the myonemes, *m*. (The other intracellular structures—nucleus, vacuoles, etc.—are omitted from the figure.)

Cilia or *flagella* are found in many protozoa and free-swimming algae: these structures serve as effectors of mechanical response, and probably also as receptors, especially for contact stimuli, since they come first into contact with external objects. Many protozoa, especially ciliates, have intracellular contractile fibrils, called *myonemes*, which effect the contraction of the whole cell or some part of it (Fig. 75). Many ciliates also have other intracellular fibrils, connecting the bases of the cilia, which are supposed to be specialized conductors, serving to coordinate the movements of the cilia. The "eye spots" of red pigment, found in many flagellates and swimming algae, seem to be especially sensitive to light, thus serving as photo-receptors (Figs. 30, 36).

Responsive mechanisms of plants.—Plants, in general, have much less highly developed responsive mechanisms than animals. This difference is obviously correlated with the fundamental difference in mode of nutrition of these two groups of organisms: plants, not having to move about to secure their food, have less need of rapid and coordinated responses.

The most rapid responses of plants are those of certain insectivorous plants, such as the Venus Flytrap (*Dionaea*) and Sundews (*Drosera*). The leaves of these plants respond quickly to contact stimuli by closing up; thus they capture insects which light on them. The leaves of the Sensitive Plant (*Mimosa*) respond to mechanical or other kinds of stimuli by folding up and drooping. Tendrils of climbing plants also respond fairly rapidly (within a minute or two) to contact stimuli. In the insectivorous plants, the receptors are special sensitive hairs on the upper surface of the leaf; in the other cases mentioned the general epidermal cells seem to act as receptors. The conduction of the excitation is chiefly through the sieve-tubes (p. 167), in which the protoplasm is continuous from cell to cell. This wave of excitation is evidenced by an electrical response (action current), and can be abolished by anaesthetics, just as in the nerves of animals. The mechanical response is effected, in all these cases, by changes of turgor (p. 85) in certain cells. The increased permeability of the plasma membrane which accompanies the state of excitation allows some of the dissolved substances to escape from these cells; this results in a decrease of osmotic pressure within the cells, with a consequent escape of water and loss of turgor, which causes the movements. These mechanical effectors are easily seen in the Sensitive Plant, where they consist of a small cushion of cells (called a *pulvinus*) at the base of each leaflet and of the main leaf-stalk. The turgor of these cells, due to their internal osmotic pressure, supports the weight of the leaf. When they lose their turgor, on excitation, the leaf droops. In the insectivorous plants there is, in addition to the mechanical response, a secretory response: special gland cells in the leaf secrete hydrolyzing enzymes which digest the captured insects.

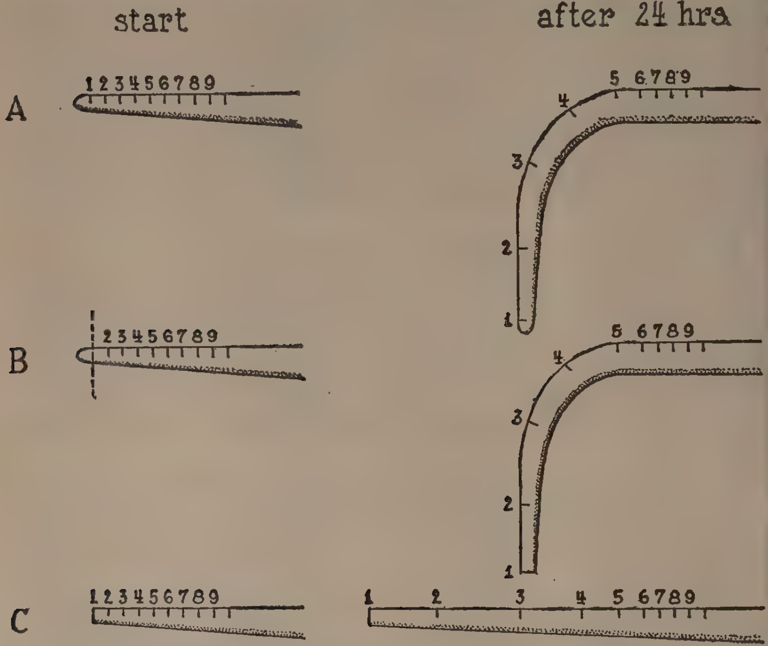


FIG. 76.—Geotropism (response to gravity) of growing roots. *A:* a root marked at intervals of 1 mm. from the tip and laid in a horizontal position; the visible response (bending), as shown at the right, occurs in the region of maximum longitudinal growth, a few millimeters behind the tip. *B:* the tip of the root was cut off, at the point indicated by the dotted line, 30 minutes *after* it was laid in the horizontal position; the response nevertheless occurs normally, as shown at the right, the stimulus having already been received before the tip was removed. *C:* the tip was cut off *before* the root was laid in the horizontal position; no bending occurs, as shown at the right, showing that the stimulus must be received at the tip, although the visible response occurs further back.

Most of the responses of plants are much slower than those just described. The most general mechanical responses of plants are *growth movements*—changes in direction of growth—in response to light, gravity and other external stimuli (moisture, heat, contact, etc.). The receptors of these stimuli are cells at the extreme tip of the growing stem or root, while the mechanical response is effected by the cells in the region of elongation (growth in length), which is some distance behind the tip, the intervening cells acting as conductors (Fig. 76). The reception, conduction, and response are all very slow: a matter of minutes or hours. The mechanical response is effected, directly, by turgor movements: decreased turgor of the cells on the side stimulated results in the bending of the stem or root toward this side; this bending is later fixed by the hardening of the cell walls as these cells become mature.

Other movements of plants—the turning of leaves toward or away from the source of light, the "explosion" of certain kinds of seed capsules, the opening and closing of stomata (p. 174), the "sleep" movements of leaves and flowers, etc. —are also effected by turgor changes in special cells.

The responsive mechanisms of Hydra exemplify, in their simplest forms, the types of receptors, conductors, and effectors found in all higher animals: sensory, nerve, muscle and gland cells. The muscular structures of this animal consist, not of separate cells, but of specially differentiated parts of the general epithelial cells: the *muscle-processes* (Fig. 77). These are elongate contractile extensions of the bases of the cells, lying next to, and partly embedded in, the mesogloea (intercellular layer). The muscle processes of the ectoderm cells extend lengthwise of the body and the tentacles; those of the endoderm crosswise. The contraction of the former therefore shortens the animal; that of the latter decreases the diameter of the body and tentacles and thus lengthens them. Within the muscle-processes are intracellular fibrils extending lengthwise of the process. These *myofibrils* are the distinctive and effective structures of all muscle cells; it is their contraction, when stimulated, which causes the shortening of the muscle cell (or, in this case, the muscle-process), with consequent movement of the animal or some part of it. Another type of mechanical effectors, peculiar to Hydra and its relatives, are the *nettle-cells*. These are distributed throughout the ectoderm, but are especially abundant on the tentacles and hypostome. They serve as weapons of both offense (food getting) and defense. The *flagella* of the endoderm cells may be considered a third type of mechanical effectors. Specialized *gland cells* are found only in the endoderm, where they lie, singly, among the ordinary epithelio-muscular cells. There are two distinct kinds of gland cells: the *slime cells*, found only in the mouth region, which secrete mucus; and the *albumin cells*, distributed throughout the endoderm, which are thought to secrete digestive enzymes. Besides these specialized types of effectors, many of the epithelial cells of

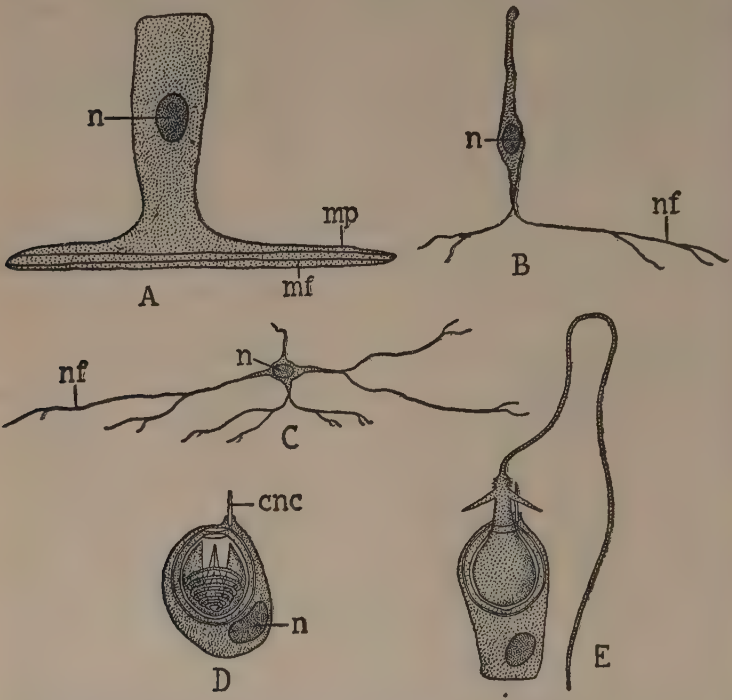


FIG. 77.—Special responsive cells of Hydra. *A*, epithelio-muscle cell; *B*, sensory cell; *C*, nerve cell; *D*, nettle-cell, undischarged; *E*, nettle-cell after discharge. *n*, nucleus; *mp*, muscle process; *mf*, myofibrils; *nf*, nerve fibers; *cnc*, cnidocil or trigger-hair, whose tactile stimulation causes discharge of the nettle-cell. (*D* and *E* after Schneider.)

both layers are capable of amoeboid movement and of secretion. The nettle-cells, the flagella, and the gland cells of Hydra are *independent effectors; i.e.*, they respond directly to external stimuli (mechanical or chemical), without the intervention of separate receptors or conductors. The epithelio-muscular cells can also function in this way, since each such cell is in direct contact, at one end, with the external surroundings or the cavity of the enteron; thus the free end of the cell may act as a receptor, while the basal (muscular) end acts as an effector (Fig. 78, *A*). These cells can also transmit excitation, rather slowly, from one to another, thus acting also as conductors.

The specialized receptors, or *sensory cells*, are very slender cells, crowded in between the epithelial cells. They are found chiefly in the mouth region of both layers, and on the foot. Those of the endoderm usually have flagella at their free ends. The most distinctive structural feature of the sensory cells is the fine branching fibers which extend out from their basal ends, making contact with the muscle-processes and with the similar fibers of other sensory cells and nerve cells. Thus these cells act not only as receptors but also as conductors, transmitting their excitation rapidly to several or many muscle-processes, which are thus stimulated simultaneously. A sensory cell communicating directly with one or more muscle-processes constitutes a *receptor-effector* system (Fig. 78, *B*).

There are also specialized *nerve cells*, whose sole function is conduction of excitation. These are found in both cell layers, though more abundantly in the ectoderm, lying between the bases of the epithelial cells. They are branching cells, with numerous very long slender processes or *nerve fibers*. The fibers of each cell unite with those of other nerve cells and of the sensory cells to form a continuous network lying on, and in close contact with, the layer of muscle-processes. This network of nerve fibers transmits excitation rapidly, thus serving to *coordinate* the movements of the animal; *i.e.*, to stimulate all the muscle processes of one cell layer, or part of it (*e.g.*, one tentacle, or one side of the body), to contract simultaneously. This type of coordinating mechanism, called a *nerve-net*, is the simplest form of *nervous system*. The nerve-net is a *diffuse* nervous system; *i.e.*, it extends throughout the whole body of the animal, and transmits excitation in all directions from any point stimulated. Nerve cells as well as sensory cells are, however, most abundant in the region about the mouth, suggesting a beginning of *centralization* of the nervous system.

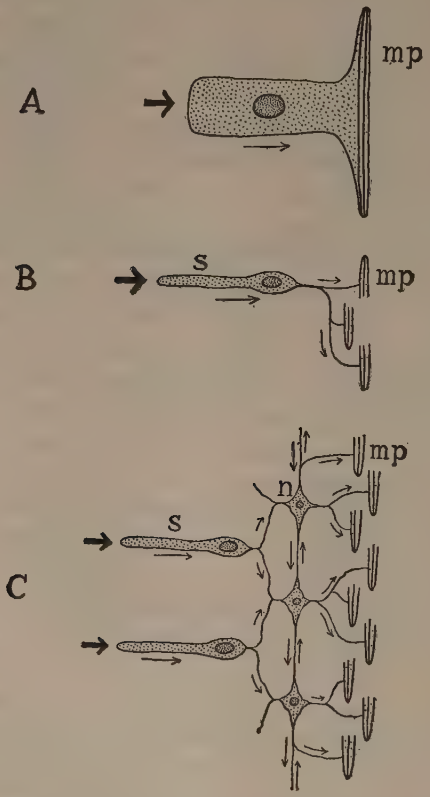


FIG. 78.—Diagrams of sensory-neuro-motor mechanisms of Hydra. *A*, independent effector (an epithelio-muscle cell stimulated directly at its free end); *B*, receptor-effector system; *C*, receptor-conductor-effector system. *mp*, muscle processes; *s*, sensory cells; *n*, nerve cells. Arrows indicate the points of external stimulation and the directions of transmission of excitation.

Sensory cells, nerve-net, and muscle-processes, together, constitute a *receptor-conductor-effector* system (Fig. 78, *C*). Such a system, as compared with simpler forms of responsive mechanisms (independent effectors or receptor-effector systems), is capable of stimulation by a greater number and variety of stimuli, of more rapid and extensive transmission of excitation, and consequently of more complex and efficient responses.

The responsive mechanisms of the earthworm are considerably more specialized and complex than those of Hydra—particularly the muscular and nervous systems. The muscles, which constitute the greatest part of the body of the animal, are composed of highly differentiated *muscle cells:* elongate, spindle-shaped cells with intracellular myofibrils running lengthwise of the cell (Fig. 83, *A*). These muscle cells are packed closely together in sheets or bundles, forming *muscle tissue.* The greatest bulk of the muscles of the earthworm are those composing the body-wall. These are arranged in two layers: an outer layer, next to the skin, of *circular* muscles, and an inner layer of *longitudinal muscles* (Fig. 58). The contraction of the latter shortens the body; that of the circular muscles decreases the diameter of the body, thus lengthening it. The ordinary locomotion of the worm is effected by the alternate contractions of these two sets of muscles. This mode of progress is aided by the *setae*, small bristles of non-cellular substance (chitin) which project through the body wall. The inner ends of the setae are connected to each other and to the body wall by small muscles whose contraction bends the setae forward or backward. When the setae project backward, the worm moves forward; when the setae project forward, the worm moves backward. The wall of the enteron contains two much thinner layers of muscle tissue: an inner layer, next to the endoderm, of circular muscles, and an outer layer of longitudinal muscles; their alternate contractions effect the movement of food along the enteron. Numerous small muscles extend from the pharynx to the body wall; their contraction effects the dilation of the pharynx, which sucks food in through the mouth. Smaller masses of muscle tissue, or scattered muscle cells, are found in the walls of the larger blood vessels, the terminal portions of the nephridia, and other internal organs.

Another type of mechanical effectors are the *cilia*, which line the intestine, parts of the nephridia, and some other internal cavities.

The *glands* of the earthworm are mostly single cells, as in

Hydra. The skin contains numerous mucus-secreting gland cells; the lining of the enteron contains both mucus cells and others which secrete digestive enzymes. Other, more complex glands are the *calciferous glands* which secrete calcium carbonate into the esophagus, and the *setigerous glands* which produce the setae.

The ciliated cells are entirely independent effectors, and the gland cells are probably also largely so. But the muscles are, normally, stimulated only through the nervous system. Muscles are quite capable of direct stimulation (*e.g.*, by electrical stimuli), though less sensitive than sensory cells or nerves; but in the intact animal, under its normal conditions of life, they never come into direct contact with external stimuli. The effects of external stimuli reach the muscles by way of specialized receptors and conductors.

The *receptors* of the earthworm are single cells as in Hydra. These sensory cells are thickly distributed throughout the skin, most abundantly in the anterior part, which is therefore the most sensitive part of the worm. Other sensory cells are present in the lining of the enteron, at least in the mouth and pharynx, and probably also in other internal organs. None of these sensory cells communicate directly with effectors, as they do in Hydra. Each sensory cell gives off, at its inner end, a single long nerve fiber which runs inward to the central nervous system (Fig. 81).

The *nervous system* of the earthworm is of an entirely different type than that of Hydra. The nerve cells, instead of being distributed throughout the body, are aggregated into definite masses, called *ganglia*. The most important of the ganglia constitute the *central nervous system*, which contains the great majority of the nerve cells of the animal. In the earthworm, the central nervous system consists of a series of closely connected ganglia (a double ganglion, or pair of ganglia, in each segment), forming a continuous cord of *nerve tissue*, composed of nerve cells and their fibers. This nerve cord extends throughout the length of the worm, lying within the body cavity on the ventral side, except at the anterior end, where it bends upward, around the enteron, to the dorsal side. There are a number of smaller ganglia in various parts of the body, outside the central nervous system; their relations and functions are probably similar to those of the autonomic ganglia of vertebrates (Ch. XVI). From the central nervous system *nerves* extend to all parts of the body. Each nerve consists of a large number of *nerve fibers*, some of which are processes of sensory cells running *in* to the central nervous system, while others are processes of nerve cells within the central nervous system running *out* to effectors.

The nerve cells are of several different forms, most of which agree in having a single very long nerve fiber, called an *axon;* many have, in addition to this, one or more shorter branching processes called *dendrites*. The whole nerve cell, with its axon and dendrites, is called a *neurone*. The sensory cells of the earthworm, described above, are also neurones: these are called *sensory neurones;* their axons, which carry nerve-impulses (*i.e.*, waves of excitation) *to* the

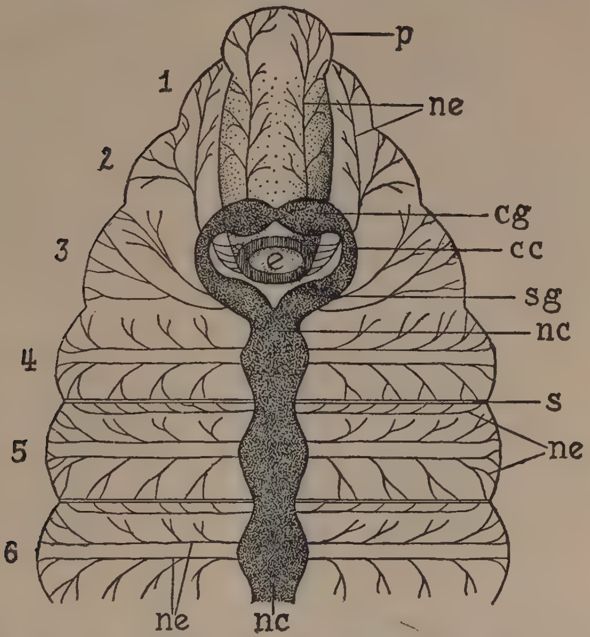


FIG. 79.—Anterior portion of the nervous system of the earthworm. *cg*, cerebral ganglion; *cc*, circum-pharyngeal commissure; *sg*, sub-pharyngeal ganglion; *nc*, ventral nerve cord; *ne*, nerves. *p*, prostomium or "upper lip"; *e*, enteron, cut off at this point to show the ventral nerve cord, which lies below it; *s*, septum. Numbers indicate the body-segments; all the posterior segments are similar to the last ones shown.

central nervous system, are called *afferent* fibers. Within the nerve cord, the ends of the afferent fibers branch freely and make contact with the dendrites of other neurones; this point of contact is called a *synapse*. Most of the neurones in the nerve cord send axons out to the muscles: these are called *motor neurones;* their axons, which carry nerve impulses *from* the central nervous system, are called *efferent* fibers. The ends of the efferent fibers make contact with muscle cells; this point of contact is called the *myo-neural junction.*

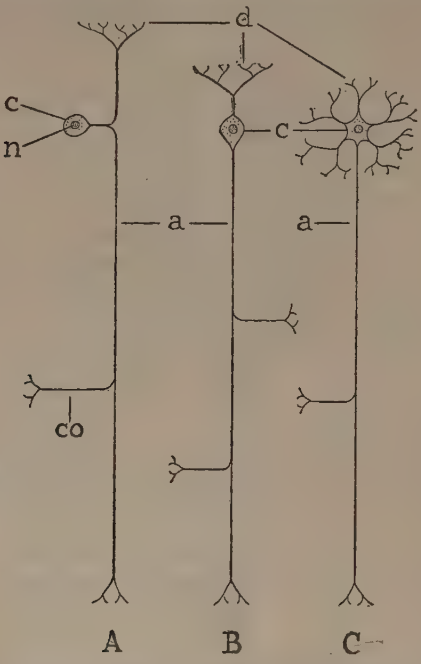


FIG. 80.—Neurones: *A*, unipolar type; *B*, bipolar type; *C*, multipolar type; many variations of these three types occur in various animals. *c*, centron or cell-body; *n*, nucleus; *d*, dendrites; *a*, axon; *co*. collateral or side-branch of the axon.

Every muscular response to an external stimulus therefore involves at least three cells: (1) a *sensory neurone*, located in the skin (or elsewhere in the body), whose axon transmits excitation in to the central nervous system, where it stimulates (2) a *motor neurone*, whose axon transmits excitation out from the central nervous system to (3) a *muscle cell*. which contracts. Such a response is called a *reflex;* and each such pathway for transmission of excitation in to the central nervous system and out to an effector is called a *reflex arc* (Fig. 81, *A*). In fact, practically every stimulus excites a number of receptors, and therefore throws

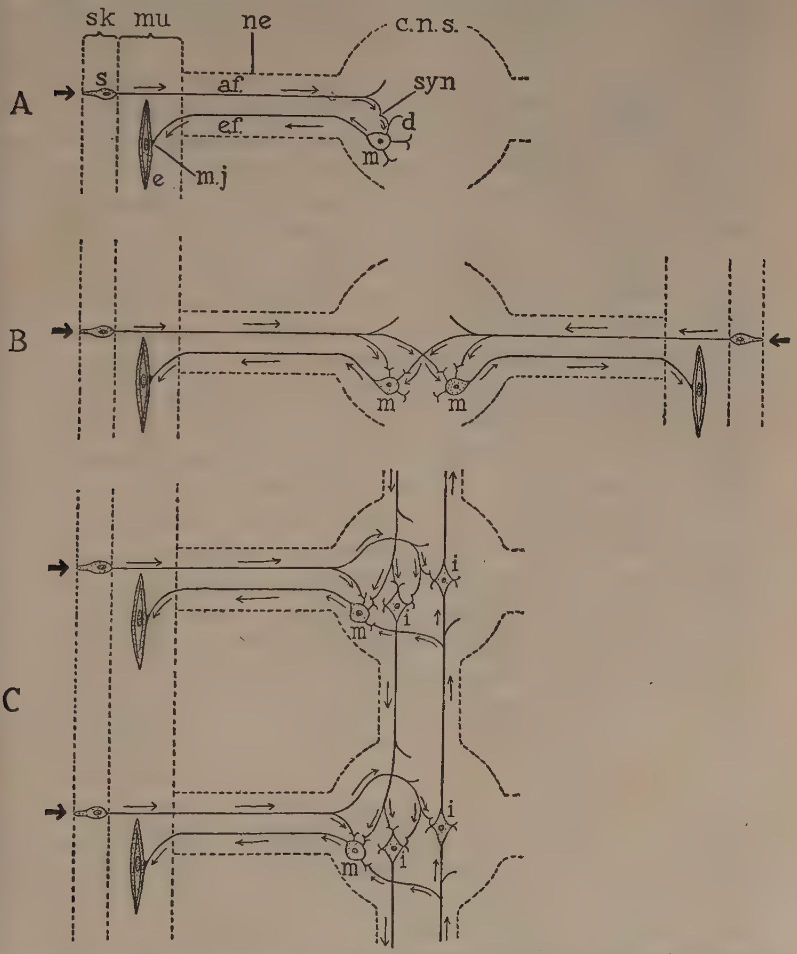


FIG. 81.—Diagrams of sensory-neuro-motor mechanisms of the earthworm. *A*, simple reflex arc; *B*, interconnected reflex arcs within a single segment, involving only sensory and motor neurones; *C*, intersegmental reflex arcs, involving intermediate neurones. *s*, sensory neurone; *a.f.*, afferent fiber; *syn*, synapse; *d*, dendrites; *m*, motor neurone; *e.f.*, efferent fiber; *m.j.*, myo-neural junction; *e*, effector (muscle cell). *i*, intermediate neurone. *sk*, skin; *mu*, muscle layer; *ne*, nerve; *c.n.s.*, central nervous system. Each ganglion, of course, actually contains a large number of neurones, and the branchings and interconnections of the neurones are actually much more complex than indicated in the diagram.

a number of reflex arcs into action simultaneously. Each sensory neurone, moreover, may make contact, through the terminal branches of its axon, with several motor neurones; and each motor neurone may be in contact, through its dendrites, with several sensory neurones (Fig. 81, *B*). These branches of a sensory or of a motor neurone are usually confined to the part of the nerve cord in a single segment of the worm. Simple reflex arcs, such as described above, therefore subserve chiefly *segmental reflexes*, *i.e.*, responses confined to the segment stimulated. There are, however, in the nerve cord, besides the motor neurones, *intermediate neurones* whose fibers do not pass out of the central nervous system, but run backward and forward within the nerve cord, serving to connect neurones in one segment with those in another (Fig. 81, *C*). Each intermediate neurone rarely extends over more than two segments, but the nerve-impulse, by being "relayed" from one to another of them, may be transmitted the whole length of the cord. Thus, by the intercalation of one or more intermediate neurones, within the central nervous system, between the primary sensory and motor neurones, longer and more complex reflex arcs are formed, subserving *intersegmental reflexes* which may involve several or many segments or even the whole body. The receptor-conductor-effector mechanism of the earthworm, and of all higher animals, is made up of a large number of reflex arcs of various lengths and variously interconnected.

The *cerebral ganglia* forming the anterior end of the central nervous system of the worm are scarcely sufficiently larger or more important than the other ganglia of the cord to be called a "brain." The receptors are, however, more numerous at this end of the animal, particularly the more specialized ones such as photo-receptors and chemoreceptors; so that these anterior ganglia probably receive more numerous and varied stimuli than other parts of the nervous system. This represents a beginning of *cephalization*, *i.e.*, concentration of sensory and nervous systems at the head end of the animal—the end which ordinarily comes first into contact with many important features of the external environment.

The responsive mechanisms of higher animals (molluscs, arthropods, and vertebrates) are of the same general type as those of the earthworm, but more specialized and complex in many details. We shall merely mention briefly here the chief "improvements" of these mechanisms in the more complex animals, especially the vertebrates, as compared with the earthworm. The structures and functions of these specialized responsive organs will be treated more fully in the following chapters.

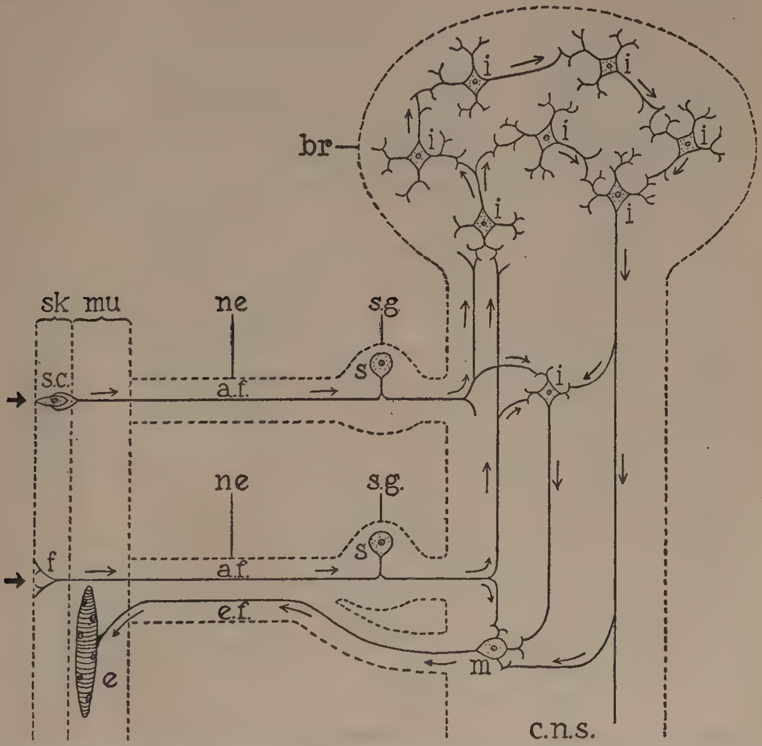


FIG. 82—Diagram of sensory-neuro-motor mechanisms of a vertebrate, including segmental and intersegmental reflex arcs and "long paths" through the brain (some of these paths are shown in more detail in Fig. 106). *f*, free nerve ending (dendrites of sensory neurone); *s.c.*, special sense cell, in contact with dendrites of sensory neurone; *s.g.*, sensory ganglion (actually containing many sensory neurones); *br*, brain; other letters as in Fig. 81.

Effectors.—The *muscles* are more specialized and differentiated into several types, and their arrangement in the body is also more complex (p. 260). The *glands* are mostly multicellular structures, under the control of the nervous system (p. 274). Other special types of effectors—luminous organs, electric organs, and pigmentary effectors (p. 279),—found in some of these animals, are also under nervous control. Certain types of effectors, however, especially ciliated cells, remain strictly independent effectors even in the highest animals.

Receptors.—Most of the receptors of higher animals are specialized *sense cells* or multicellular *sense organs*, distinct from the sensory neurones (Ch. XV). The cell-bodies of the sensory neurones usually do not lie in the sensory surface (as they do in the earthworm) but in special *sensory ganglia* within the body, whence they send fibers out to the sense organs and in to the central nervous system (Fig. 82).

Cephalization.—The most specialized sense organs—those of sight, hearing, smell, and taste—are usually all located in the head, which is therefore the chief region for reception of external stimuli. Correlated with this, the front end of the central nervous system is greatly enlarged and differentiated, forming the *brain*, which, especially in the higher vertebrates, comes to dominate all the responsive mechanisms of the body.

"*Long paths.*"—The central nervous system in all higher animals, just as in the earthworm, contains the cell-bodies of most of the motor neurones whose axons run out to the muscles. But the great majority of the neurones in the central nervous system of the higher vertebrates are *intermediate neurones* whose fibers lie entirely within the central nervous system, connecting up its various parts. The nervous system of the highest animals is made up, like that of the earthworm, of a large number of reflex arcs connecting receptors with effectors; but many of these neural paths, especially those involving the brain, are very long and complexly interconnected (Ch. XVI). These extremely numerous and intricate neural connections form the basis of the complex behavior of the higher animals, culminating in man.

CHAPTER XIV

EFFECTORS

EFFECTORS are organs, cells, or differentiated parts of a cell, which carry out some special type of response producing some external effect. The chief types of effectors, found in most organisms, are *mechanical effectors*—mechanisms of movement—and *glands*—mechanisms of secretion. Besides these, there are special types of effectors, found in only a limited number of organisms, such as electrical organs, luminous organs, and chromatophores.

The chief types of externally effective *movements* of cells are *muscular*, *ciliary*, *amoeboid*, and *turgor* movements; there are also various kinds of purely *intracellular* movements of protoplasm.

Muscles have been studied more than any other type of effector. This study has thrown a great deal of light on the mechanisms of other types of response, and also on certain very general aspects of excitation and cell metabolism.

The effective movement of a muscle is always *contraction*, *i.e.*, shortening. What we call contraction of a muscle is merely a change in shape, not in volume, of the muscle cells; *i.e.*, they become shorter and thicker. Muscle tissue is usually composed of elongate cells all extending in the same direction: the simultaneous shortening of these cells effects an extensive and forcible shortening of the whole muscle, which may do external work, *e.g.*, move the organism or some part of it, lift a weight, etc. The *relaxation* of the muscle—return to its original length after contraction—is a relatively passive process, incapable of doing external work. The essential contractile elements in the muscle cell are the *myofibrils*, intracellular strands of relatively solid protoplasm extending longitudinally through the cell; the more liquid cytoplasm between the fibrils is called *sarcoplasm*.

The simplest structures which may be called muscular are the contractile fibrils (*myonemes*) found in many protozoa, which look and act like the myofibrils of differentiated muscle cells: their shortening, on stimulation of the organism, effects a change in shape of the cell or some part of it (Fig. 75). The least differentiated type of muscular structure in multicellular animals is exemplified by the epitheliomuscular cells of Hydra (p. 247). In these, only part of each cell is specialized for contraction, containing myofibrils; the rest of the cell is like an ordinary epithelial cell. The differentiated muscle tissues of higher animals comprise three distinct types (Fig. 83):

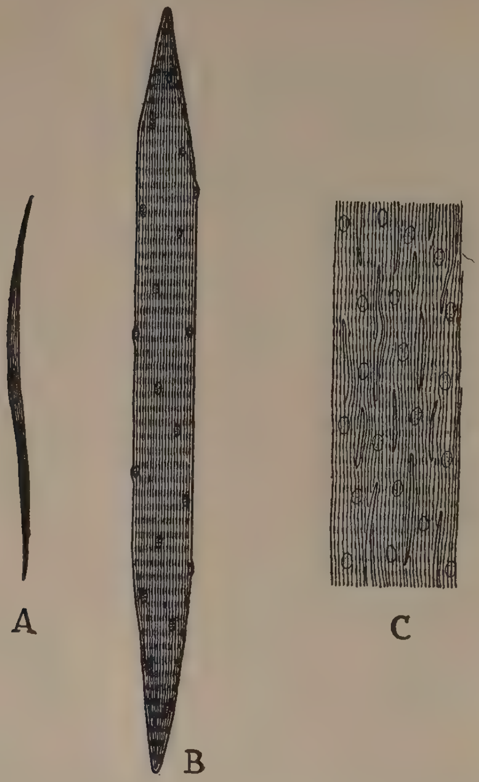


FIG. 83.—Muscle cells. *A*, a smooth muscle cell; *B*, a skeletal muscle fiber; *C*, a small piece of cardiac muscle tissue.

(1) *Smooth muscle* is the least specialized type of muscle tissue. This is the only type found in some invertebrates, such as the earthworm, where it forms the musculature of

the body wall as well as the internal organs. In the vertebrates, this type of muscle is found chiefly in the nutritive organs—digestive, circulatory (except the heart), excretory, etc. Smooth muscle is composed of small spindle-shaped cells, each with a single nucleus in the center; the cytoplasm is differentiated into myofibrils and sarcoplasm. These cells are often arranged in layers of considerable thickness, all the cells extending in one direction; *e.g.*, the circular and the longitudinal muscle layers of the intestine (Fig. 66). In other cases they are scattered singly or in small groups among other tissues.

(2) *Skeletal muscle* is the type composing the musculature of the body wall and limbs of vertebrates, and is also found in many invertebrates (molluscs, arthropods, etc.). This tissue is composed of cylindrical *muscle fibers*, which may be as long as 4 or 5 cm. Each fiber is a multinucleate cell, or syncytium (p. 33). The nuclei usually lie just beneath the surface membrane. The cytoplasm is composed of myofibrils and sarcoplasm, as in smooth muscle cells. In skeletal muscle, however, each myofibril is made up of alternate light and dark segments, which occupy corresponding positions in all the fibrils of a fiber, giving the whole fiber the appearance of transverse striation. The muscle fibers are bound together by connective tissue, forming large bundles of definite size and shape; each of these bundles is what we call "a muscle." The skeletal muscles of vertebrates are usually attached to *bones*, by means of *tendons*, tough strands of connective tissue. In most cases, the two ends of a muscle are attached to different bones, which articulate with each other by a flexible joint. The muscles are often arranged in opposing pairs, one muscle (*flexor*) to bend the joint and another (*extensor*) to straighten it. Joints which are capable of movement in more than one plane, such as the shoulder and hip joints, have a number of muscles to bend them in various directions. In many invertebrates, the skeletal muscles are attached to the inside of a jointed *exo-skeleton*, or shell.

(3) *Cardiac muscle* is peculiar to the vertebrate heart. This tissue appears to be made up of uni-nucleate cells with central nuclei, like smooth muscle. The cells of cardiac muscle are not really separate, however, but are connected

with each other by anastomosing branches, so that there is direct protoplasmic continuity throughout the tissue; the whole heart is therefore, in effect, a single huge syncytium. The myofibrils have the same structure as those of skeletal muscle, so that cardiac muscle also appears cross-striated.

These three types of muscle tissue are also called by the following names:

$$\begin{array}{lll} \text{striated} = \left\{\begin{array}{l}\text{skeletal}\\ \\ \text{cardiac}\end{array}\right. & \begin{array}{l} = \text{“voluntary”} \\ \\ \\ \end{array} \\ \text{smooth} = \;\; \text{visceral} & \end{array} \qquad \left.\begin{array}{l}\text{cardiac}\\ \text{visceral}\end{array}\right\} = \text{“involuntary”}$$

Corresponding to the differences in structure, there are certain characteristic differences in the action of these three types of muscle. Striated muscle acts more rapidly than smooth muscle: the contraction and relaxation, following a single stimulus, takes 0.1 second or less in skeletal muscle; from 0.3 to 2 seconds in cardiac muscle; and from 3 seconds to 3 minutes in smooth muscle. The cross-striation of the more rapidly acting muscles may represent a segmented structure of the myofibrils which prevents them from rupturing during their very rapid shortening.

In skeletal muscle, under normal conditions, the state of excitation does not spread from one muscle fiber to others; so that while each individual fiber responds in accordance with the all-or-none law (p. 243), the muscle as a whole is capable of various degrees of contraction, according to the number of fibers stimulated. Each muscle fiber is connected with a separate efferent nerve fiber and is, normally, stimulated only through this. The skeletal muscles are therefore capable of finely graded and precisely controlled movements. In smooth muscle, the state of excitation is transmitted from cell to cell (p. 239), so that a "wave" of contraction travels along the tissue from any point stimulated. In cardiac muscle, where there is direct protoplasmic continuity throughout the tissue, the state of excitation is transmitted very rapidly, so that the whole heart contracts practically simultaneously. The heart as a whole therefore responds in an all-or-none manner; *i.e.*, any stimulus which excites it at all arouses the maximum contraction of which the heart is capable at the moment.

The most striking characteristic of cardiac muscle is its automatic rhythmic contraction, which is displayed not only by the whole heart, but by small isolated pieces of heart tissue, and even by single cardiac muscle cells grown outside the body. Smooth muscle often shows automatic rhythmic contractions also, though much slower (from 1 to 12 contractions per minute). Skeletal muscle can be made to act in this way only by immersing it in a solution containing sodium but no calcium ions. The beating of the heart also depends on the kinds and proportions of the various cations (Na^+, K^+, Ca^{++}, Mg^{++}) present in the surrounding fluid. The differences among the three types of muscle in this respect seem to be merely differences of degree in their sensitiveness to direct stimulation by ions. The rhythmic character of the response is due to the refractory period, as previously explained (p. 241).

A type of direct stimulation to which smooth muscle is especially susceptible is *stretching.* The tissue responds to a pull by contracting; if the external tension be continuous, the tissue often shows rhythmic contractions.

The normal activities of skeletal muscle depend entirely on stimuli received through efferent nerve fibers; if its nerves are cut, the muscle relaxes completely. A sustained contraction of this type of muscle is due to rapidly recurring stimuli (about 50 per second). This type of sustained contraction, called a *tetanus*, involves a continuous expenditure of energy; the muscle sooner or later becomes *fatigued* and relaxes. Smooth muscle, however, is able to maintain a state of contraction, once attained, without further stimulation; once it has shortened to any particular extent, it tends to "stay put" at that length indefinitely, and apparently without any further expenditure of energy; this condition is called *tonus.*

In general, we may say that the activity of skeletal muscle—under natural conditions, in the body of the animal—is entirely dependent on impulses from the central nervous system; smooth muscle displays a certain amount of independent activity, manifested in tonus, response to stretching, rhythmic and wave-like contractions; while the heart is essentially an independent effector, whose activity is merely modified by nervous stimuli.

The mechanism of muscular movement has been most extensively studied in the skeletal muscles of vertebrates, especially those of the frog. When a skeletal muscle is stimulated, either directly or through its nerve, with a single stimulus (*e.g.*, the making or breaking of an electric current), it gives a single short sharp contraction and returns quickly to its original form. The whole duration of this *muscle twitch* may be 0.1 second or less. Nevertheless, by means of appropriate apparatus, it is possible to analyze this process into three periods: (1) the *latent period*, from the application of the stimulus to the beginning of the visible (mechanical) response, 0.01 second or less; (2) the *contraction period*, during which the muscle shortens, about 0.04 second; (3) the *relaxation period*, during which the muscle returns to its original length, about 0.05 second. The visible response is followed by (4) the *recovery period*, evidenced by consumption of oxygen, production of carbon dioxide, and liberation of heat (Fig. 84). If the muscle be stimulated repeatedly at intervals shorter than the normal duration of its recovery period, it becomes *fatigued*—incapable of normal response.

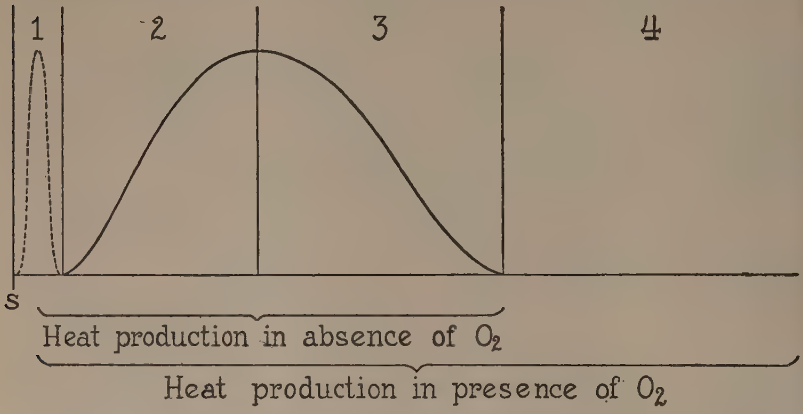


FIG. 84.—Diagram illustrating analysis of muscle twitch. The dotted line represents the electrical response (change of electrical potential), the heavy line the mechanical response (contraction and relaxation) of the muscle. *s*, moment of stimulation; *1*, latent period; *2*, contraction period; *3*, relaxation period; *4*, recovery period. (Adapted from Hogben.)

During the latent period, between the moment of stimulation and the beginning of the mechanical response, occurs the electrical response, which, as we have seen (p. 238), is the indication of the state of excitation. The electrical response always precedes the mechanical response. The state of excitation seems to "set off" the chemical reactions underlying the mechanical response. We might conceive that the action current itself acts like a "spark" to initiate the "explosion" of some fuel substance in the cell. A more probable explanation is that it is not the electrical change itself but the increased permeability which accompanies it that initiates the chemical reaction. As pointed out before (p. 240), it is very probable that this increase of permeability, due to some structural change in the protoplasm, is not confined to the plasma membrane but extends more or less throughout the cell. This may permit the mixing of substances—*e.g.*, a fuel substance and an enzyme catalyzing its decomposition—previously separated by intracellular membranes impermeable to them. There is every reason to suppose that metabolic processes in general are regulated by such changes in protoplasmic structure. At any rate, mechanical responses (and other types of special responses) always do *follow* the state of excitation indicated by the electrical response.

The contraction of the muscle liberates energy—both mechanical energy and heat—which must come from some "downhill" chemical reaction in the cell. The mechanical response occurs perfectly normally in the complete absence of oxygen; the reaction supplying this energy is therefore not an oxidation. If a muscle which has been repeatedly caused to contract in the absence of oxygen be chemically analyzed, it is found to contain a considerable quantity of *lactic acid* (p. 113); this substance is practically absent in the normal resting muscle. Moreover, for every gram of lactic acid so produced, 0.9 gram of *glycogen* has disappeared from the muscle. The normal resting muscle cells always contain a considerable amount (1–3%) of glycogen as a stored fuel substance (p. 214). Glycogen is readily converted into glucose by hydrolysis, and glucose into lactic acid by a series of reactions (p. 113) not involving oxidation. These reactions may be represented in a simplified form thus:

$$\begin{array}{cccc} C_6H_{10}O_5 & +\; H_2O & \rightarrow C_6H_{12}O_6 & \rightarrow 2\,C_3H_6O_3 \\ \text{glycogen} & \text{water} & \text{glucose} & \text{lactic acid} \\ 0.9\text{ g.} & 0.1\text{ g.} & 1\text{ g.} & 1\text{ g.} \end{array}$$

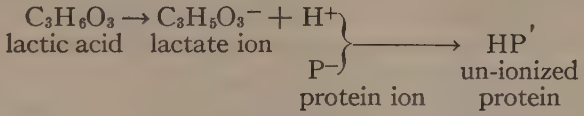
The intermediate steps and the catalysts involved do not here concern us, as these do not affect the amount of energy liberated (p. 154). The potential energy[1] of 1 gram of lactic acid is a little less than that of 0.9 gram of glycogen; this difference must be liberated, as some form of kinetic energy, in the reaction. Moreover, the lactic acid, as fast as it is formed, reacts with other substances, chiefly proteins, in the cell; this reaction (neutralization) also liberates energy. The energy liberated by the muscle, as mechanical energy and heat, can be very exactly measured, and is found to be exactly equal to that calculated from these reactions; thus:

		Calories
Total energy liberated by muscle (in absence of oxygen) per g. of lactic acid produced		.370
Potential energy of 0.9 g. glycogen	3.836	
Potential energy of 1 g. lactic acid	3.601	
Difference = energy liberated by conversion of glycogen to lactic acid	.235	
Energy liberated by neutralization of 1 g. lactic acid by protein	.135	
TOTAL	.370	.370

If these chemical reactions took place in a structureless system—*e.g.*, completely ground-up muscle tissue—all the energy would be liberated as heat. But in the intact muscle, a large proportion of this energy appears as mechanical energy, capable of doing external work, such as lifting a weight. To transform chemical into mechanical energy requires some kind of physical machinery (p. 14). Calculations based on the physical laws applying to different kinds of machines indicate that the only possible mechanism which would give the amount of mechanical energy actually developed by a muscle, per gram of lactic acid produced, is an electrical one. This mechanism may be conceived to operate in the following manner: Every muscle cell (or muscle fiber), as we have seen, contains longitudinal intracellular fibrils. These myofibrils are composed chiefly of protein material, with a definite physical structure; *i.e.*, in a fairly solid, or firm gel, state. The fibril must be held together, as every solid or semi-solid substance is, by cohesive forces—intermolecular attractions—between its molecules. But, under the normal conditions in the cell (*i.e.*, in a neutral medium) the proteins exist chiefly as anions (p. 52). The electric charges on these protein ions tend to push them apart (p. 7). The balance between these two opposing forces—molecular cohesion and electrostatic repulsion—determines the normal length of the fibrils in the resting muscle cell. The glycogen must be largely concentrated on the surfaces of these fibrils; the lactic acid is therefore formed at these surfaces. Lactic acid, being a fairly strong acid, is largely ionized as soon as it is formed; the hydrogen ions thus produced combine immediately with the protein anions. These reactions may be represented thus:

---

[1] By this is meant the total energy which would be liberated by the complete combustion of this amount of the substance to CO_2 and H_2O.

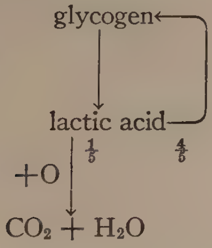


$$\left.\begin{array}{r} \underset{\text{lactic acid}}{C_3H_6O_3} \rightarrow \underset{\text{lactate ion}}{C_3H_5O_3^-} + H^+ \\ \underset{\text{protein ion}}{P^-} \end{array}\right\} \longrightarrow \underset{\substack{\text{un-ionized}\\ \text{protein}}}{HP'}$$

It will be seen that this reaction abolishes (or greatly reduces) the electric charges on the protein ions composing the fibril; the cohesive forces therefore pull these protein molecules closer together, shortening the fibrils: this causes the contraction of the muscle. This action of acid on a protein structure can be easily shown artificially: thin strands of catgut immersed in acid shorten quickly and extensively; such changes are capable of exerting enormous forces, and, like the contraction of the muscle, are completely reversible and can be repeated indefinitely.

The fibrils are surrounded, in the cells, by a larger amount of more liquid protoplasm—the sarcoplasm—which also contains proteins capable of neutralizing acid, *i.e.*, combining with hydrogen ions. The lactic acid and its ions therefore rapidly diffuse away from the surface of the fibrils into the surrounding sarcoplasm; the reaction represented above, on the surface of the fibril, is largely reversed, and the fibrils return to their original condition: the muscle relaxes. The time required for this diffusion process, in the microscopic spaces between the fibrils—not more than a few thousandths of a millimeter—is only a few millionths of a second; the chemical reactions involved are also practically instantaneous. The mechanical changes of contraction and relaxation lag, to a certain extent, behind the chemical and electrical changes, because the muscle, like any mechanical system, has a certain amount of inertia.

None of the reactions so far described, it will be noted, involve oxidation; the contraction and relaxation of the muscle will take place perfectly normally, for a number of times, in the complete absence of oxygen. But, as the muscle continues to respond, it gradually becomes "saturated" with lactic acid, and the cell protoplasm can then neutralize no more acid: the fibrils are therefore unable to return to their original condition after shortening. If we continue to stimulate the muscle, in the absence of oxygen, the relaxation becomes slower and incomplete; finally the muscle fails to respond at all, remaining in a partly contracted condition: it is completely fatigued. Nor will it ever recover from this state of fatigue, no matter how long we allow it to rest, without oxygen. But if we furnish the fatigued muscle with an adequate supply of oxygen, it will, in time, recover its normal responsiveness. During this recovery oxygen is consumed, carbon dioxide is produced, and heat is liberated. When the muscle has completely recovered, we find by chemical analysis that the lactic acid has completely disappeared from it. As we know that lactic acid is oxidized in cells to CO_2 and H_2O, with the liberation of energy (p. 113), the inference is obvious that the lactic acid has been removed by oxidation. But if all the lactic acid were completely oxidized, it is obvious from the figures given above (p. 266) that the heat produced during the recovery period should be almost ten times as great as the total energy liberated during the preceding mechanical response. We find, however, that the heat liberated during recovery is only about equal to, or a little greater than, the total energy liberated during the contraction and relaxation. It is known, in fact, that the greater part of the lactic acid is not oxidized, but is converted back into glycogen. This is an "uphill" reaction requiring energy, which is supplied by the oxidation of part of the lactic acid. About 1/5 of the lactic acid is oxidized: of the energy thus liberated, about half is utilized in the re-synthesis of glycogen from the remaining lactic acid, while the other half is "wasted" as heat. When the muscle contracts under normal conditions—with an adequate oxygen supply—this recovery process probably begins immediately upon the first appearance of lactic acid, but takes longer to complete than the mechanical response. Under these circumstances the muscle does not become fatigued unless the successive responses are too close together to allow sufficient time for completion of the recovery process, *i.e.*, the complete removal of lactic acid. The relations between the chemical reactions of response and recovery may be represented thus:



The muscle, as a mechanism for transforming chemical into mechanical energy, is comparable in certain respects to a storage battery running an electric motor: in each case, the energy liberated by a chemical reaction is transformed into mechanical work by way of electrical changes; in each case, the system when "discharged" must be "recharged" by another process which restores its potential energy—a recovery process.

The recovery process in the muscle is only about 50% efficient; *i.e.*, only about half the energy of oxidation is converted into potential energy in the cell, the other half being wasted as heat. The efficiency of the contraction process itself depends on mechanical conditions, such as the extent of stretching of the muscle at the beginning of contraction, the load it has to lift, and the speed of contraction. Under ideal conditions, the absolute mechanical efficiency of the contraction process may be at least 90%; *i.e.*, nine-tenths of the energy liberated by the chemical reactions may appear as mechanical energy in the muscle. Not all of this mechanical energy, however, can be converted into external work; part of it is inevitably dissipated in internal friction in the muscle, as in any machine. The *net* working efficiency of muscles, in practice, is probably never more than 25–33%; *i.e.*, not more than one-fourth to one-third of the total energy liberated in the whole cycle of muscular activity—including the recovery process—is obtained as useful work: the rest is degraded into heat during contraction, relaxation, and recovery.

We may summarize as follows the processes involved in muscular activity, remembering, of course, that some of these processes overlap in duration:

Internal events		*External events*	
excitation	→	electrical response	latent period
decomposition of glycogen to lactic acid on surfaces of fibrils	→	heat	
ionization of lactic acid			
combination of H^+ with protein of fibrils	→	heat	contraction period
shortening of fibrils	→	contraction	
diffusion of lactic acid from fibrils to sarcoplasm			
return of fibrils to original condition	→	relaxation	relaxation period
neutralization of lactic acid by proteins of sarcoplasm	→	heat	
oxidation of 1/5 of lactic acid	← → →	absorption of O_2 production of CO_2 heat	recovery period
re-synthesis of 4/5 of lactic acid to glycogen			

Ciliary movement.—This term may be used to include the activities of *cilia* and *flagella*, which seem to be essentially similar in structure and probably in the intrinsic mechanism of their movements. Cilia differ from flagella chiefly in being smaller, more numerous, and acting more coordinately. Flagella are found in many bacteria, flagellates, unicellular algae, the sperm cells of higher organisms, and some multicellular tissues such as the endoderm of Hydra. Cilia are found in the ciliate protozoa and many epithelial tissues of higher animals, such as the ectoderm of Planaria, intestine and nephridia of the earthworm, respiratory passages of vertebrates, etc. In unicellular organisms these structures effect movement of the cell itself; in multicellular tissues, movement of liquids or small particles over the surface of the tissue.

Cilia act by bending rapidly and forcefully in one direction, then relaxing and returning more slowly to their original position (Fig. 85). In most ciliated epithelia, the effective stroke is always in the same direction; in the protozoa, it may be reversed temporarily. In flagella, the effective movement, at least in many cases, seems to be a whirling movement of the free end, which pulls or pushes the organism forward like the propeller of an airplane or a steamship.

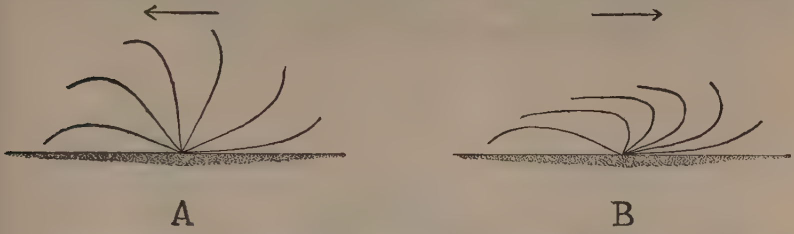


FIG. 85.—Diagram illustrating movement of a cilium: *A*, effective stroke; *B*, recovery stroke. (After Gray.)

In each cilium or flagellum there is an *axial filament* of more solid protoplasm, which is thought to be the essential contractile element, like the myofibrils of muscle cells. The inner end of this filament is usually attached to a basal granule in the ectoplasm of the cell. In ciliated cells excitation is evidently transmitted from cilium to cilium through the ectoplasm of the cell, for all the cilia beat in a regular sequence, even in a small bit of the ectoplasm removed, with its attached cilia, from the rest of the cell. In ciliated epithelia, excitation must be similarly transmitted from cell to cell, for the movement of the cilia travels forward over the whole surface of the tissue, like a wave of bending over a field of grass. These ciliated epithelia of higher animals are always independent effectors, entirely uninfluenced by the nervous system.

The mechanism of ciliary movement has been studied much less than that of muscles, but there is some evidence that its nature is fundamentally similar; *i.e.*, that the "contraction" (the effective stroke) is caused by an explosive production of acid, which is afterward removed by oxidation. Ciliary movement, like muscular activity, will continue for some time in the complete absence of oxygen, but finally stops; recovery from this state of fatigue involves the consumption of oxygen, just as in the muscle.

Amoeboid movement is the type of movement exhibited by Amoeba and many other protozoa, and by the leucocytes, or "wandering cells," found in all higher animals. In these cells, such movements effect both locomotion and ingestion of solid particles (*phagocytosis*). Many other kinds of animal cells—connective tissue cells, epithelial cells, etc. —also effect phagocytosis in the same way.

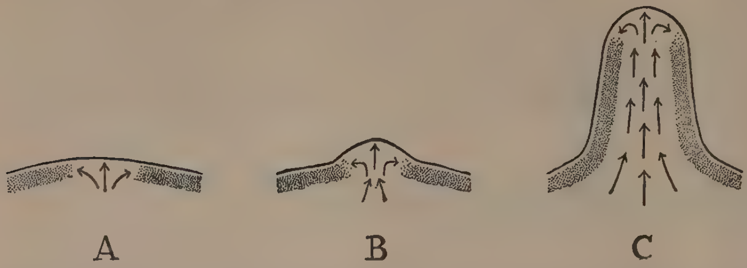


FIG. 86.—Diagrams illustrating formation of pseudopodium: *A*, *B*, *C*, successive stages. The shaded areas represent the more solid protoplasm, the unshaded areas the more fluid portions; the arrows indicate direction of flow of the fluid protoplasm. (*C* after Chambers.)

This type of movement is effected by the formation and withdrawal of temporary projections of the protoplasm, called *pseudopodia* (Fig. 26). These movements can be strikingly imitated in very simple liquid systems, such as a drop of mercury or of chloroform in water. In such drops, locomotion, ingestion, and egestion, closely resembling these processes in Amoeba, can be induced by chemical substances or by electric currents which produce changes in *surface tension* at the surface of the drop. The physical conditions at the surface of an amoeba are, however, much more complex than in these simple two-phase liquid systems. For there is not merely a single phase-boundary between the external water and the protoplasm of the amoeba, but the latter is itself a physically complex system of many phases (p. 72); surface tension phenomena at these internal surfaces must be at least as important as those at the external surface. Moreover, the ectoplasm, in the resting state, is not liquid, but a rather firm gel. The first visible change in the formation of a pseudopodium is a liquefaction of the ectoplasm at one point, followed by an outflowing of the protoplasm at this point (Fig. 86). This might be regarded as a decrease of surface tension at this point, but it is probable that the physical forces involved are more complex than those usually included in the term "surface tension." There is direct evidence that this liquefaction is preceded by an increase of acidity in the protoplasm at this point. This would suggest that the chemical mechanism of amoeboid movement may be fundamentally similar to that of muscular movement, though the physical machinery is quite different.

Turgor movements are the chief mechanism of mechanical responses in plants. These movements are most easily seen in rapid responses, such as that of the Sensitive Plant; but the same mechanism seems to be involved in the slower responses usually called "growth movements." The mechanism of this type of movement has been described previously (p. 245); it seems to be but a special case of the increase of permeability which always accompanies excitation. The potential energy which is transformed into movement in this case is the elasticity of the protoplasm and cellulose wall of the turgid cell. But to restore the cell to its turgid condition after the response requires energy, which must be supplied by some "downhill" metabolic process, presumably oxidation. So, even here, we find some resemblance to the muscle system: an "explosive" mechanism of high potential energy which is "discharged" by excitation and "recharged" by an oxidative recovery process.

Intracellular movements are of many kinds, some of which are responses to external stimuli, while others seem to be "spontaneous," *i.e.*, dependent primarily on internal conditions and processes of the cell. These spontaneous activities of the protoplasm can, however, be modified by external stimuli. One of the most general types of intracellular movement is the protoplasmic streaming readily seen in many plant cells and protozoa, and also present in many metazoan cells, though less conspicuous. This movement can be particularly well studied in the large internodal cells of Nitella (p. 159). The result of any effective external stimulus—mechanical, electrical, etc.—is sudden *cessation* of the streaming movement. This is preceded by an electrical response, which is transmitted from the point of stimulation in the usual way (p. 239). The cessation of movement is therefore evidently the response to excitation in this case. This response is effected by a gelation of the protoplasm, as shown by the fact that Brownian movement—always present in any liquid system—also ceases simultaneously. This response may very possibly be of the same nature as that of the myofibrils of the muscle cell—due to the electrical discharge of the protein anions by hydrogen ions (p. 267).

The very complex intracellular movements involved in cell division will be described later (Chapter XVIII).

Secretion may be defined as the liberation, either to the outside of the cell or into vacuoles, of substances synthesized or accumulated by the cell. In this broad sense, secretion is one of the most universal life processes. Typical secretory processes are exhibited by unicellular organisms (protozoa, bacteria, yeasts, etc.) and by many types of cells in multicellular organisms (epithelial cells, leucocytes, connective-tissue cells, etc.). But in all multicellular animals, and also in many plants, there are cells or organs specialized for the synthesis and secretion of particular substances. These special secretory effectors are called *glands*.

Glands may be single cells or multicellular organs (Fig. 87). Unicellular glands—specialized secretory cells distributed singly among the ordinary epithelial cells—are common in the lower invertebrates (Hydra, earthworm, etc.), and even in the vertebrates unicellular mucus glands occur in all mucous membranes. But most of the glands of higher animals are multicellular structures. Such glands are composed of specialized epithelial tissue most of whose cells are secretory cells. These multicellular glands, with very few exceptions, originate as invaginations of the surface epithelium of the body or of hollow organs, and most of them retain their connections with these surfaces by way of *ducts*, through which their products are secreted to the outside of the body or into the cavity of the enteron: all such glands (as well as the unicellular glands previously mentioned) are called glands of *external secretion*. There are some other glands which have no ducts, either having lost them in the course of development or (in a very few cases) having originated in an entirely different way; these ductless glands secrete their products into the blood: such are called glands of *internal secretion.* A few glands—*e.g.*, the pancreas—have both an external secretion (into the enteron) and an internal secretion (into the blood): the two secretions consist of entirely different substances and are produced by different cells which are, accidentally, so to speak, included in the same organ.

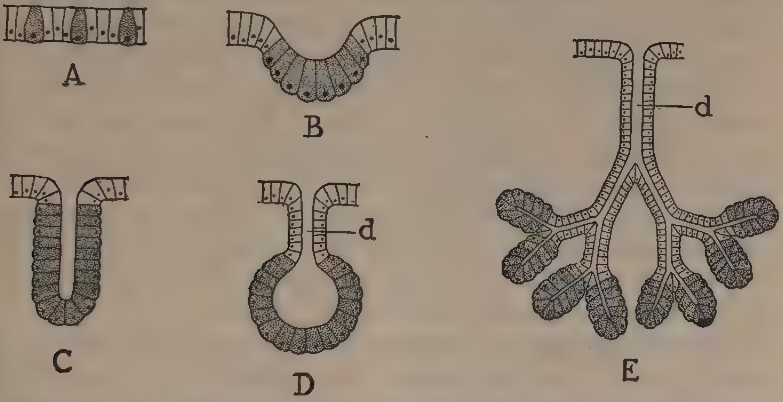


FIG. 87.—Diagrams of the structure of glands; the actual gland-cells are shaded in each figure. *A*, single gland-cells scattered among ordinary epithelial cells; *B*, a very simple multicellular gland, consisting of a group of gland-cells lining a slight invagination of the epithelium; *C*, a simple tubular gland; *D*, a simple alveolar gland; *E*, a compound tubular gland (large glands, such as the liver and pancreas, are of this type, but with thousands of secreting tubules); *d*, duct.

The most distinctive visible intracellular feature of most gland cells is the presence of *secretory granules*, composed of the special products of the cell which are stored in this form until their discharge. In some cases these special products may replace practically the whole of the ordinary cytoplasm. These secretory substances appear in the cytoplasm, but the nucleus plays an essential rôle in their production, as in all constructive activities of the cell (p. 23). The nucleus of gland cells is often very large and irregularly shaped—lobed, branched, or even divided—so that it has a very extensive surface of contact with the cytoplasm (Fig. 9). Some gland cells have *intracellular* *canals*—narrow, branching vacuoles—which may open to the exterior and through which the secretion may be discharged.

Some glands secrete continuously, though their spontaneous activity may be modified by stimulation, either direct or nervous. Many glands, however, discharge their products only in response to stimuli. In some of the lower animals all the glands are strictly independent effectors, susceptible only to direct stimulation; this is also true of some glands even in the highest animals. But most of the glands of vertebrates are under control of the nervous system, though many of them are normally subject also to chemical stimulation by substances in the blood (Ch. XVI).

The kinds of substances secreted by glands, and their functions in the general economy of the organism, are of enormous variety: digestive enzymes; protective substances, such as mucus and sebum; poisons, which serve for both defense and offense (food getting); skeletal substances; building materials, such as silk; nutrient fluids, such as milk; and many others. The internal secretions of the ductless glands will be discussed later (Chapter XVI).

The mechanism of secretion.—The activities of most glands involve two processes: the *synthesis* of the specific products, and their *discharge* from the cells. The term "secretion" is often used to include both these processes. The two are related, essentially, as the mechanical response and the recovery process in muscle: the discharge of the gland cell is its "explosive" response to a stimulus, like the contraction of a muscle cell; the synthetic reaction is part of the recovery process which "recharges" it, like the synthesis of glycogen in the muscle cell. We are here concerned primarily with the mechanism of the discharge, which is the special response of the gland to a stimulus.

Of the two types, internal and external secretion, the former seems to be the simpler. In this case, the product of the special synthetic metabolism of the gland cells has merely to escape into the surrounding lymph and thence into the blood. This would seem to be simply a process of diffusion. This may occur continuously, it may be accelerated by stimulation, or it may occur only on stimulation. These effects of stimulation can probably be interpreted as due to the increased permeability accompanying excitation (p. 239), which would facilitate the diffusion of dissolved substances from the cell.

The process of external secretion is more complex. The characteristic feature of this process is that the secretion is discharged from the cells always *in one direction;* namely, into the duct. The special products of the gland (enzymes, etc.) form only a small fraction of the secretion, whose most abundant component is *water.* Since the gland cells show only a slight diminution in volume after secretion, this water must come chiefly from the body-fluids behind the cells, *i.e.*, on the side away from the duct (Fig. 88). The essential character of the act of external secretion is therefore the creation of a current of water from the blood and lymph through the gland cells into the duct; this water contains more or less of the salts (and other diffusible components) of the blood plasma, and carries out the special products of the gland cells with it. The most probable mechanism of the production of this current is an increase of osmotic pressure in the cell, together with increased permeability of the free end of the cell next to the duct. An increase in the cell, on stimulation, of osmotically active substances, to which the membrane at the basal end of the cell is impermeable while the free end is permeable, must result in such a current as long as these conditions are maintained (Fig. 89). This increase of osmotic pressure may be produced by the dissolution of the secretory granules themselves or by the decomposition of some food substance in the cell, like the decomposition of glycogen to lactic acid in the muscle cell, producing a larger number of dissolved molecules; it will be

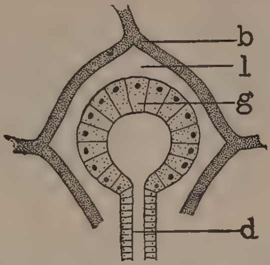


FIG. 88.—Diagram showing the relation of a gland to blood vessels and lymph spaces. *b*, blood capillary; *l*, lymph space; *g*, gland-cells; *d*, duct.

recalled that osmotic pressure is proportional to the number of dissolved molecules (p. 81). The greater permeability of one end of the cell during secretion is shown not only by the visible result—*i.e.*, that the secretion flows in this direction—but also by the electrical response. There is a difference of electrical potential, during secretion, between the two ends of the gland cell—*i.e.*, between the duct and the back of the gland—indicating a difference of permeability to ions (p. 239). This structural change in the free end of the gland cell must, in many cases, be more extensive than an "increase of permeability," in the usual sense; for the secretory granules are often carried out bodily into the secretion, indicating a complete disintegration of the cell surface at this end. In some gland cells, such as mucus cells, the rupturing of the free end is very obvious, and the greater part of the cell contents is carried out into the secretion.

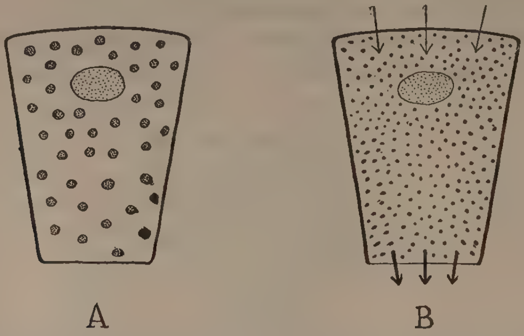


FIG. 89.—Diagram illustrating the mechanism of secretion. *A*, the resting gland-cell; *B*, the gland-cell excited: the increase of osmotic pressure, together with increased permeability (or complete breakdown) of the membrane on the duct side of the cell, causes a flow of water from the lymph space through the cell, carrying its secretion out into the duct.

The act of secretion obviously involves an expenditure of energy. This energy is furnished, as in other effectors, indirectly by oxidation. But in glands, just as in muscles, it is found that the consumption of oxygen occurs, chiefly at least, after the visible response, and continues for some time after the cessation of active secretion. This clearly indicates the probability that in glandular, as in muscular and ciliary, activity the chemical reactions during the response are non-oxidative decompositions, while oxidations furnish the energy for "recharging" the cells during the recovery period. There is also evidence that the substance oxidized in glands, as in muscles, is carbohydrate or some fragment of carbohydrate decomposition, such as lactic acid. Thus the chemical mechanism of secretory response may be fundamentally very similar to that of mechanical response, although the external effects are so different.

Pigmentary effectors, or *chromatophores*, which effect changes of color, are found in many animals (crustacea, molluscs, fishes, amphibia, and reptiles). These color changes may be regarded as special cases of mechanical response, since they all involve movements of cells or of pigment granules within the cells. The chromatophores of molluscs are multicellular structures operated by muscles. Those of vertebrates are single amoeboid cells, in which the color change is effected by extension and withdrawal of pseudopodia or by streaming movements within the cells (Fig. 90). When these pigmented cells are in the contracted condition the color of the animal is lighter; when they are expanded it is darker. They may be stimulated in various ways, directly or through the nervous system; the response to a stimulus is always contraction. The normal stimulus, at least in many cases, is *light*, acting through the eyes and the nervous system; thus in light-colored surroundings, which reflect more light, the chromatophores are contracted and the color of the animal is lighter; while in darker surroundings they expand and the animal becomes darker. The normal response is abolished by destroying the eyes, the afferent nerves from the eyes to the central nervous system, or the efferent nerves to the chromatophores; thus a

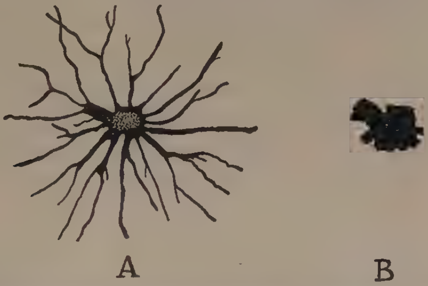


FIG. 90.—Chromatophores containing black pigment, from the scales of a fish (Fundulus): *A*, expanded; *B*, contracted. (After Spaeth.)

blind fish is often sharply distinguishable from its normal fellows by its permanently dark color.

Electric organs are found in several kinds of fishes. These organs are highly modified muscles or glands, in which the mechanical or secretory response has been lost entirely, leaving only the electrical response. The normal mode of stimulation is through nerves. The organ is composed of disc-shaped cells arranged in columns, with the efferent nerve endings on one side of each cell—the same side in all the cells of the organ. Thus when they are stimulated, the potential difference between the stimulated and the unstimulated side of the cell (p. 239) is in the same direction in all the cells. The result is the same as in a battery of galvanic cells connected in series: the electro-motive forces of all the individual cells are summated. The total electromotive force thus developed by these organs is as great as 450 volts in some cases. The current produced is a rhythmic series of discharges, in one direction only, each single discharge lasting about 0.005 second. These organs serve their possessors as weapons of attack and defense.

Luminescence—the production of light—occurs in many kinds of organisms. In luminous bacteria and fungi the light production is continuous, but in most luminescent animals it occurs only in response to stimulation. In some cases the luminous material is a secretion, produced by unicellular glands; but in the more specialized types of luminescent organs (found in various insects, crustacea, molluscs, and fishes) the light production is intracellular. The light is produced by oxidation of an organic substance called *luciferin* by the catalytic action of a specific enzyme called *luciferase*. The luciferins and luciferases of different animals are probably not identical. In some cases the luciferin produces light when oxidized by inorganic oxidizing agents. The light-producing reaction is reversible; *i.e.*, the oxidation product of luciferin can be converted back into luciferin by reducing agents. The light is not produced by high temperature, as in most artificial lighting devices, but by direct transformation of chemical energy into light. The amount of heat produced in bio-luminescence is therefore relatively very small.

Heat production.—According to the Second Law of

Energy p. (14), in every energy transformation some fraction of the energy is degraded into heat and thus "wasted"; *i.e.*, converted into a form from which it can not be converted back into other forms. This is just as true of all life processes as of non-living processes; or, to put the same thing in another way, no living mechanism is 100% efficient in transforming chemical energy into mechanical, osmotic, electrical, or light energy—there is always a certain "leakage" of energy as heat. In many kinds of artificial machines, heat is an essential part of the mechanism; as, for instance, in the transformation of chemical into mechanical energy in a steam engine, or of electrical energy into light in an incandescent lamp. This is not true of any living mechanism: the heat produced by these is not an intermediate step in the main energy transformation, but simply a by-product.

In most organisms this heat production represents a pure waste of energy; but in the two highest classes of vertebrates, the birds and mammals, it is utilized to maintain a high and uniform body temperature (p. 218), which enables the metabolism of these animals to proceed at a relatively high and uniform rate (p. 95) regardless of the temperature of their surroundings. There are no special effectors for heat production in these "warm-blooded" animals: heat is produced by all the organs in proportion to their size and activity; the muscles, comprising the greatest bulk of active tissue, produce most of it. The constancy of the body temperature is maintained by the regulation, through the nervous system, of both heat production and loss of heat from the body. When the outside temperature is low, the tension of the muscles increases, producing more heat (p. 264); an extreme form of this is *shivering.* When the outside temperature is high, muscular tension decreases, and also the rate of heat loss from the body is increased by several mechanisms: more blood flows through the blood vessels of the skin, increasing the dissipation of heat to the air; the *sweat glands* secrete, causing loss of heat by evaporation; *panting* increases heat loss by increasing evaporation of water from the lungs, respiratory passages, and mouth. All these responses are reflexes through special temperature receptors in the skin (p. 291) and a special temperature-regulating center in the central nervous system (p. 318).

CHAPTER XV

RECEPTORS

Receptors are organs, cells, or differentiated parts of a cell, which are especially susceptible to particular kinds of stimuli. The special function of a receptor is to be excited by some external force impinging directly upon it, and to transmit this excitation to an effector, which is thereby aroused to activity. In the simplest cases receptors may be in direct contact with effectors, but in higher animals the excitation is transmitted through one or more nerve cells interposed between receptor and effector. In many cases, the receptor itself is a special type of nerve cell (sensory neurone), which acts as both receptor and conductor; but in most of the multicellular sense organs of higher animals, the receptor cells are specialized epithelial cells distinct from, but in close contact with, the sensory neurones (Fig. 82).

All living cells are probably sensitive, to a greater or less degree, to electrical, mechanical, osmotic, thermal, and chemical stimuli. We have learned that the chemical and physical structure of protoplasm is very complex and unstable (p. 72). Its structure at any moment is determined by a delicate balance of many forces—chemical affinities, electric charges, surface tension, etc. It is not surprising, therefore, that a sudden, even though slight, change in any one of these factors may upset this balance, resulting in a temporary alteration of the structure, with consequent electrical and chemical changes, which we call the state of excitation (p. 238). A cell (or part of a cell) specialized for reception is simply one which, because of some special peculiarity of composition or structure, is unusually sensitive to one particular kind of stimulus. Whatever the external force initiating it, the excitation of the receptor results in an action current which stimulates the immediately adjacent cells, usually nerve cells; these, in turn, transmit their excitation in the same way to other cells and thus ultimately to effectors.

Stimulus and "sensation."—In ourselves, the stimulation of receptors results, in many cases, in "sensations" which can be reported verbally. The sensation is, of course, something that happens in the central nervous system, not in the receptor itself. The quality of the sensation depends, not on the nature of the stimulus nor even on the type of receptor stimulated, but solely on the connections within the central nervous system of the afferent nerve fibers which transmit the excitation. If a particular nerve be stimulated by any means whatever, at any point of its course, the resulting sensation is always the same. Normally, of course, afferent nerve fibers are excited only by their receptors, and these only by the particular kind of stimulus to which they are especially sensitive. We learn by experience, therefore, to associate a particular sensation with a particular kind of stimulus and with a particular part of the body.

We know nothing at all about the "sensations," strictly speaking, of animals that can not talk. When we speak of a "sense"—*e.g.*, touch, pain, hunger, etc.—in other animals, this is to be understood as simply a convenient short method of indicating that certain stimuli arouse responses similar to those which, in ourselves, are always associated with that particular kind of sensation. In most vertebrates the sense organs are so similar to our own that we can, with considerable certainty, infer their functions from their structure. In lower animals, however, we can usually determine the functions of particular receptors only by the responses of the animal to particular kinds of stimuli applied to them. In speaking of organisms in general, it is therefore most convenient to classify receptors according to the kinds of stimuli (p. 241) to which they are specifically sensitive.

Mechano-receptors—receptors especially sensitive to mechanical stimuli—are found in almost all animals and in some plants (p. 245). *Tactile* receptors, stimulated by contact with external objects, are present throughout the surface of the body in almost all multicellular animals, being especially abundant in projecting organs such as fingers, tentacles, proboscides, etc.; these are the receptors concerned in the sense of *touch*. Besides these, there are many internal mechano-receptors, which are stimulated by pressure within hollow organs (stomach, intestine, bladder, etc.) or by the movements of parts of the body (Fig. 91). Some of these internal receptors in ourselves arouse sensations when stimulated; but many of them initiate muscular or glandular responses which are entirely unconscious.

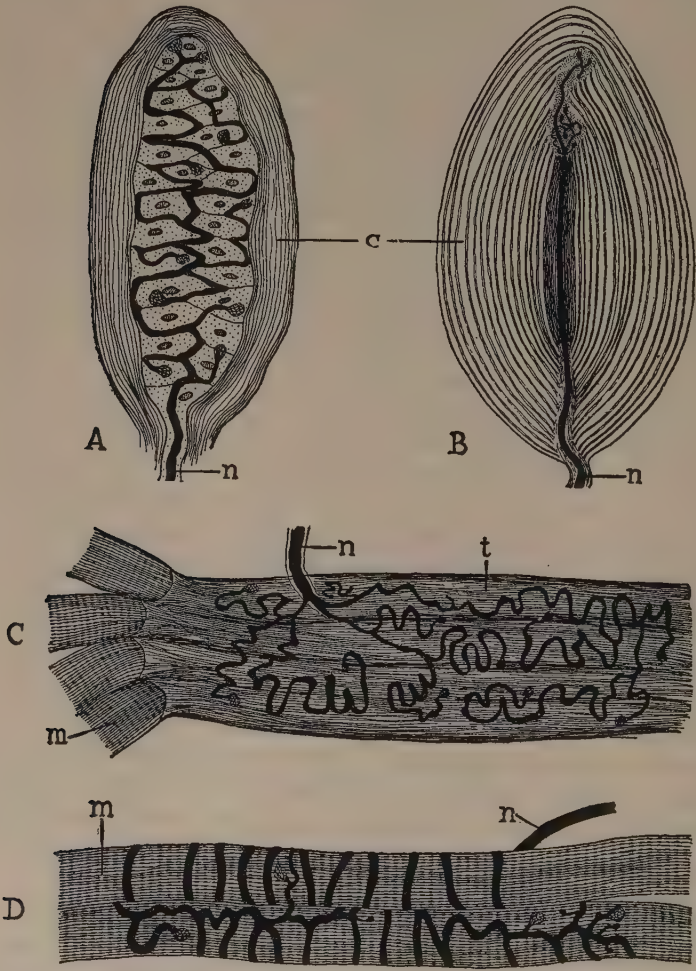


FIG. 91.—Some types of mechano-receptors of vertebrates. *A*, tactile corpuscle (touch receptor) from the skin. *B*, Pacinian corpuscle (pressure receptor), found in the deeper layers of the skin and in many internal organs. *C*, Golgi organ (proprioceptor) on a tendon. *D*, muscle spindle (proprioceptor) in skeletal muscle. *n*, afferent nerve fibers (the cell-bodies of these fibers lie in the sensory ganglia); *c*, connective tissue capsules; *t*, tendon; *m*, muscle fibers.

The receptors concerned in the sense of *hunger* are located in the walls of the stomach (in vertebrates) and are stimulated by contractions of the empty stomach. All animals must have some kind of stimulus functioning in this way, to make them seek food, but we know nothing of its nature or location in the invertebrates. The receptors concerned in the senses of *position* and *movement* of the parts of the body, called *proprioceptors*, are located in the muscles, tendons, and joints: their stimuli play an essential rôle in the coordination of the complex muscular movements involved in posture and locomotion.

Receptors concerned with *equilibrium* are found in many kinds of animals. The equilibrium organs of invertebrates are hollow cavities, called *statocysts*, lined with receptor cells having sensory hairs projecting into the cavity. Within the cavity are loose solid particles (sand grains or crystals of calcium carbonate) called *statoliths* (Fig. 92). According to the position of the animal, with respect to gravity, the statoliths press on, and stimulate, different receptor cells: these stimuli initiate responses which keep the animal "right side up." The equilibrium organ of vertebrates is a more complex structure, forming part of the inner ear (Fig. 93). The whole organ, in each ear, is called the *labyrinth:* it consists of two cavities, the *utricle* and *saccule*, and three *semicircular canals*. The utricle and saccule are similar in structure and function to the statocysts of invertebrates. The semicircular canals also contain receptor cells with sensory hairs, which are stimulated by movements of the head, or of the whole animal, in any direction.

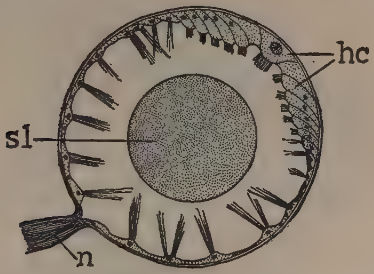


FIG. 92.—Statocyst of a mollusc (Pterotrachea). *n*, afferent nerve fiber; *sl*, statolith; *hc*, hair-cells, the actual receptors. (After Claus.)

In fishes, the ear is solely an organ of equilibrium, but in the land vertebrates part of it forms an organ of *hearing*. The essential part of the hearing organ is a portion of the inner ear called the *cochlea*. This contains receptor cells with sensory hairs (Fig. 94) which are stimulated by sound vibrations, transmitted from the external air, through the *tympanic cavity*, to the fluid in the cochlea. The perception of differences in pitch and quality of sounds depends on the fact that different receptors (hair-cells) in the cochlea are stimulated by vibrations of different frequencies. The only other animals, so far as we know, which have special organs of hearing are some insects. Their "ears" are entirely different in structure and location from the ears of vertebrates, and also differ greatly in various groups of insects.

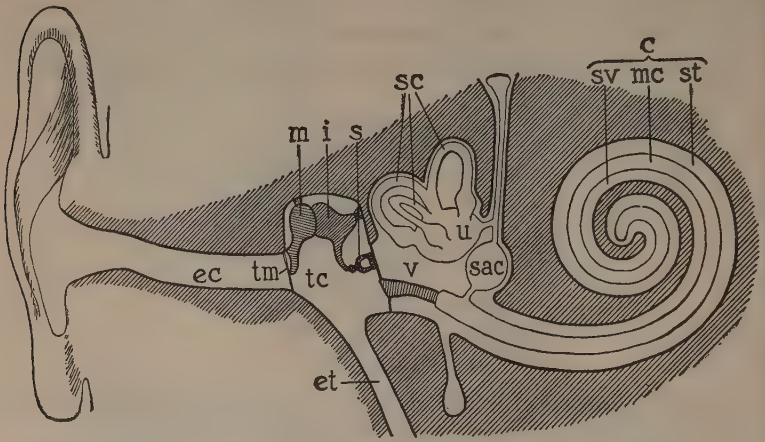


FIG. 93.—Diagram of the structure of the human ear. The shaded portions with heavy outlines represent bone, the lighter lines represent membranous structures. *ec*, external auditory canal; *tm*, tympanic membrane; *tc*, tympanic cavity; *m*, *i*, *s*, movable bones of the middle ear, which transmit vibrations of the tympanic membrane to the fluids of the inner ear; *et*, Eustachian tube, opening to the pharynx. Inner ear: *v*, vestibule; *u*, utricle; *sac*, saccule; *sc*, semicircular canals; *c*, cochlea; *sv*, scala vestibuli; *st*, scala tympani; *mc*, membranous canal. All the cavities of the inner ear are filled with fluids (lymph), which transmit vibrations.

Chemo-receptors—susceptible to stimulation by particular kinds of chemical substances—are present in almost all animals. Their primary function is the discovery and recognition of food. In the higher animals there are two distinct types of chemo-receptors, those of *taste* and of *smell.* The latter are much more sensitive, so that they are stimulated by very minute amounts of substances carried through the air or water. The taste receptors are usually located inside the mouth and stimulated only by substances actually in the mouth cavity.

The taste receptors of vertebrates are multicellular structures, called *taste buds;* the receptive cells are specialized epithelial cells, in close contact with the ends of afferent nerve fibers (Fig. 95). The smell receptors are sensory neurones whose cell bodies are located directly in the mucous membrane of the nose, their axons running in to the

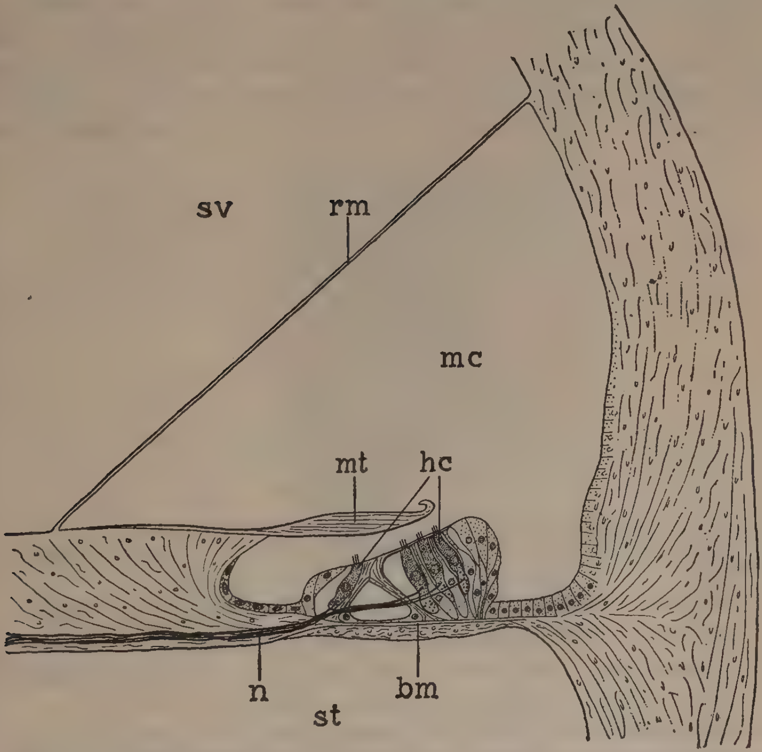


FIG. 94.—Cross-section of a portion of the cochlea. *rm*, Reissner's membrane, separating the membranous canal (*mc*) from the scala vestibuli (*sv*); *bm*, basilar membrane, separating the membranous canal from the scala tympani (*st*); *mt*, membrana tectoria; *hc*, hair-cells, the actual sound receptors; *n*, afferent nerve fibers, making up the auditory nerve (their cell-bodies lie in a sensory ganglion, not shown in the figure). Vibrations transmitted to the basilar membrane by the fluids of the cochlea cause the sensory hairs to strike the membrana tectoria, stimulating the hair-cells.

central nervous system; these are the only sensory neurones of vertebrates which have this simple relation (Fig. 96).

As in all the senses, differences in the tastes or smells of different substances depend on the fact that they stimulate different receptors and therefore excite different nerve fibers. It is easy to demonstrate that there are, in man, only four different tastes—sweet, sour, bitter, and salty—which are aroused by the stimulation of different taste buds. The number of specifically different smell receptors is probably much larger, but is very difficult to determine exactly, as the sensations combine with and modify each other (in the central nervous system) in such a way as to produce an apparently unlimited number of different smells. Many of the sensations commonly attributed to taste are actually smells or combinations of taste and smell sensations.

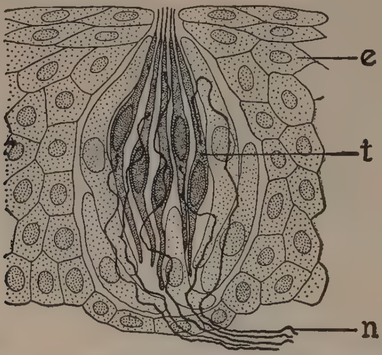


FIG. 95.—A taste bud from the tongue. *e*, epithelial cell; *t*, taste cell (receptor); *n*, afferent nerve fiber (the cell-bodies of these fibers lie in a sensory ganglion).

Photo-receptors.—Many, though not all, organisms are sensitive to light. For a cell to be stimulated by light, it must contain some *photo-sensitive* substance, *i.e.*, a substance which undergoes some chemical change when it absorbs light. Since most such substances do not absorb all wave-lengths of light equally, they are usually colored substances (p. 126); the chemical change occurring under the influence of light (*photo-chemical* reaction) often produces a change of color.

The simplest type of special photo-receptor is the red pigment spot seen in many flagellates and unicellular algae (Figs. 30, 36). Such simple "eye-spots" also occur in some multicellular animals. This simple type of photo-receptor is sensitive only to changes of intensity or color of light. An *eye*, in the proper sense of the word—*i.e.*, a photo-receptive organ capable of perception of form—is a complex organ, consisting essentially of a number of receptor cells forming a photo-sensory surface, together with a mechanism (*dioptric* mechanism) which focuses the light so as to form an image on this surface. There are many different types of eyes found in various groups of animals.

The vertebrate eye is closely comparable, in many respects, to a photographic camera (Fig. 97). The dioptric mechanism consists chiefly of the *cornea*—the convex transparent front of the eyeball—and the *lens*, located shortly behind the cornea. The focus is changed, to accommodate for near or distant objects, in the lower vertebrates by changes in the *position* of the lens, as in a camera, but in the higher vertebrates by changes in the *shape* of the lens, effected by muscles inside the eyeball. There is also a diaphragm, the *iris*—located between the cornea and the lens—which regulates the amount of light admitted to the eye by muscular movements which change the size of the *pupil*, a hole in its center. The wall of the eyeball, except the cornea, is very opaque and its inner surface is darkly pigmented, as in a camera, preventing reflection of light within it. The sensory surface of the eye is called the *retina* (Fig. 98). The actual receptors are specialized sensory neurones called *rods* and *cones*. These cells contain a photo-sensitive substance called *visual purple*, which is decomposed by light into products which cause excitation of the cell. The cones are found chiefly in the central region of the retina, the rods in the peripheral regions. The rods are stimulated by much weaker light than the cones, but are

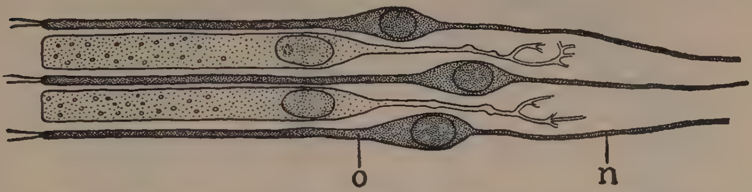


FIG. 96.—Olfactory cells from the nose. *o*, olfactory cell (smell receptor); *n*, afferent nerve fiber, the axon of the olfactory cell.

incapable of distinguishing color differences or sharp outlines. The retina contains, besides the sensory neurones (rods and cones), two "relays" of intermediate neurones, to which the excitation is transmitted, and thence through their axons to the central nervous system; this is the only sense organ which contains intermediate neurones within itself. The perception of form depends on the stimulation of receptors in different regions of the retina, with consequent excitation of different intermediate neurones and their axons. Perception of color differences is probably due to stimulation of different cones by light of different wavelengths.

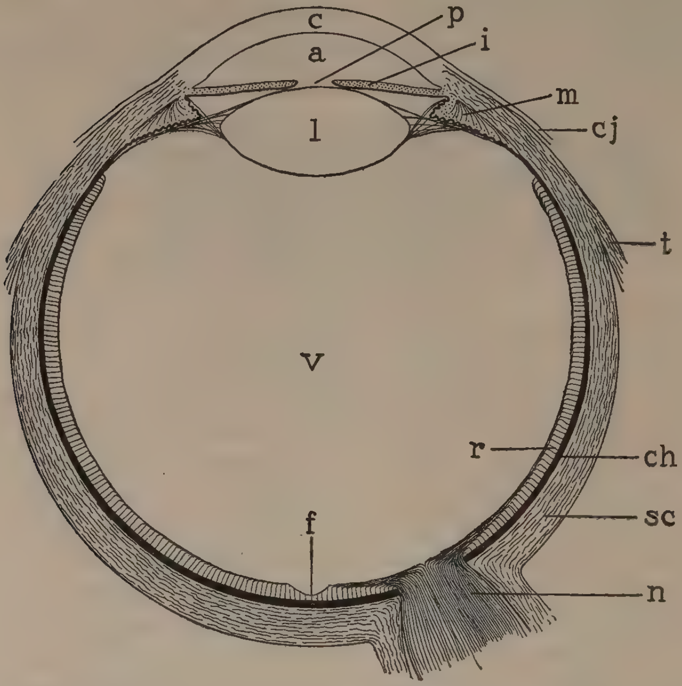


FIG. 97.—Diagrammatic horizontal section of the human eye. *c*, cornea; *a*, aqueous fluid; *p*, pupil; *i*, iris; *l*, lens; *m*, muscles controlling the shape of the lens; *cj*, conjunctiva; *t*, tendon of one of the muscles moving the eyeball; *v*, vitreous fluid; *r*, retina; *ch*, choroid coat; *sc*, sclerotic coat; *f*, fovea centralis, the region of most acute vision; *n*, optic nerve.

A very different type of eye is the *compound eye* found in many arthropods (insects, crustacea, etc.). This consists of a large number of small eyes, each with its own lens and photo-sensory cells, set closely together side by side.

Other types of receptors.—The skin of warm-blooded animals contains receptors especially sensitive to slight changes of temperature (*thermo-receptors*). The receptors stimulated by cold are distinct from those stimulated by warmth. Responses initiated by these stimuli play an important part in the regulation of the body temperature (p. 281). It is not known whether any other animals have special thermo-receptors.

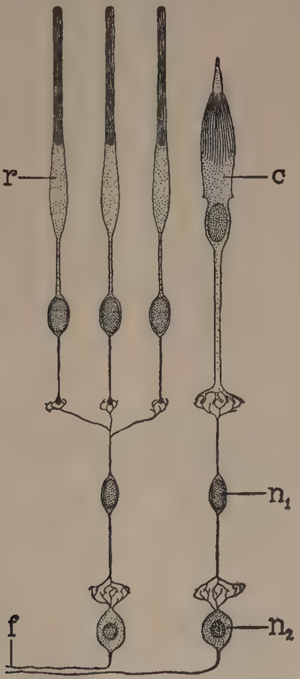


FIG. 98.—Diagram of the structure of a small portion of the retina. *r*, rod; *c*, cone; n_1, n_2, intermediate neurones of the retina; *f*, optic nerve fiber, the axon of a retinal neurone.

The special stimulus for the receptors concerned in the sense of *thirst* is probably osmotic. These receptors, in man and probably in all the higher vertebrates at least, are located in the throat. They are stimulated by increase of osmotic pressure in the surrounding fluids, which may be caused either by dryness of the throat or by insufficient water in the body as a whole. All land animals must have some kind of stimulus functioning in this way, to make them drink, but we know nothing about its location in the invertebrates.

Besides the specialized types of receptors which have been described, there are other receptors which are not especially sensitive to any particular kind of stimulus, but may be excited by any kind of stimulus provided it be very strong. The stimulation of these receptors, in ourselves, arouses the sensation of *pain*. Similar stimuli arouse in all animals responses similar to those which are associated with pain in ourselves. The receptors for these painful stimuli are, in vertebrates, *free nerve endings*, *i.e.*, the ends of afferent nerve fibers not connected with any special receptor organs (Fig. 99). To excite these, a stimulus must be strong enough to be actually injurious; it seems probable that the excitation of the nerve endings may be caused by the injury current (p. 239) of the surrounding cells. Nothing is known about the form of pain receptors, as distinct from special mechano- and chemo-receptors, in invertebrates, but their responses to injurious stimuli indicate that they must have separate receptors for such stimuli.

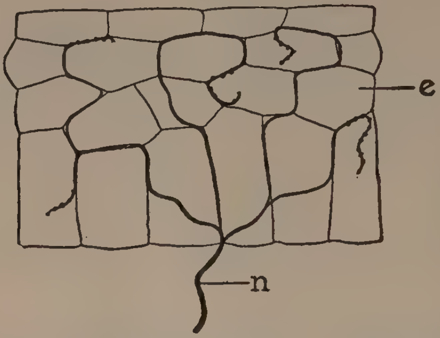


FIG. 99.—Free nerve ending in epithelium. *e*, epithelial cell; *n*, afferent nerve fiber, whose terminal branches end freely among the epithelial cells (its cell-body lies in a sensory ganglion).

There seem to be no special receptors for electrical stimuli in any organism. Nerves, muscles, and probably all other types of cells except special receptors, are more sensitive to electrical than to any other kind of stimuli.

CHAPTER XVI

COORDINATION

In a living organism the several parts work together, simultaneously or successively, in such a manner as to effect the nutrition, protection, and reproduction of the organism. The special mechanisms by which this harmonious interaction of parts is effected are called mechanisms of *coordination.*

Two distinct types of coordinating mechanisms are found in organisms: *nervous coordination* and *chemical coordination.* By nervous coordination is meant the transmission of the *state of excitation* from one cell, or part of a cell, to others. This process occurs in all organisms and all cells, but reaches its highest degree of specialization in the nervous system of higher animals. By chemical coordination is meant the transmission of dissolved *substances*, by way of the body-fluids, from one part of the organism to others, whose activities they stimulate or modify. This type of coordination has been extensively studied, as yet, only in the vertebrates, where it seems to be best developed; but there is reason to suppose that it also operates, to a greater or less extent, in many or all organisms.

Nature of the nerve-impulse.—The transmission of excitation, while a property of all living cells, is most conveniently studied in the *nerves* of higher animals, which are tissues specialized for this particular function. For this reason, the transmitted state of excitation is often spoken of as the *nerve-impulse.*

The state of excitation, as we have seen (p. 238), is a complex phenomenon, involving structural, chemical and electrical changes from the resting condition of the protoplasm. Recent studies of the nerve-impulse, in comparison with certain inorganic systems which simulate closely many of its phenomena, seem to indicate clearly that the electrical change—the *action current*—is the mechanism especially involved in the transmission of excitation from one point to another. The way in which this mechanism works is pictured, on the basis of our present knowledge, as follows: Nerves (and other tissues) can be stimulated—aroused to excitation—by many kinds of forces: mechanical, chemical, etc. In the case of nerves (and probably of all other cells except specialized receptors), however, the normal mode of stimulation seems to be electrical; *i.e.*, it requires a smaller amount of energy in the form of an electric current than in any other form to stimulate them, and they can be repeatedly stimulated without injury only in this way. From quantitative experiments on electrical stimulation, in comparison with the known laws of electrical phenomena in non-living systems, it is concluded that the stimulating effect of the current is due to the change of concentration of ions at some surface of the cell, *e.g.*, the outer or the inner surface of the plasma membrane. This alters the normal distribution of electric charges at the surface, thus upsetting the balance of forces which maintains the resting structure of the protoplasm (p. 282). The result of this upset is the series of physical and chemical changes in the protoplasm which we call, collectively, the state of excitation. Conspicuous among these changes is the change of electrical potential at the point of excitation, which produces the action current (p. 238). When a nerve (or other tissue) is stimulated by an outside—*i.e.*, artificial—electric current, it is found that excitation always occurs at the *negative electrode*, *i.e.*, at the point where the outside current tends to pull the positive ions *away from* the outer surface of the cell membrane, abolishing the normal polarization of the membrane (Fig. 100). The action current, produced by the cell itself as a result of excitation, is always in the direction opposite to this; *i.e.*, the positive ions flow *toward* the point of excitation from the outer surface of the unexcited portions of the cell. The action current therefore tends to counteract the effect of the stimulating current at the excited point, and thus aids in restoring the resting condition at this point. At the neighboring points of the cell surface, however, the action current, obviously, is in the direction tending to stimulate the cell at these points. It can also be readily demonstrated experimentally that the action current of an excited cell is sufficiently strong to stimulate a contiguous cell. A state of excitation, once aroused at any one point, therefore tends to spread in all directions from this point. The special structural peculiarity of *nerve cells*, as we have seen, is the possession of long slender fibers. In their normal position in the organism, these nerve fibers are ordinarily stimulated at only one end; the state of excitation is therefore transmitted along the fiber from its receptive end: this constitutes the nerve-impulse (Fig. 100). The speed of transmission of excitation is much greater in nerves

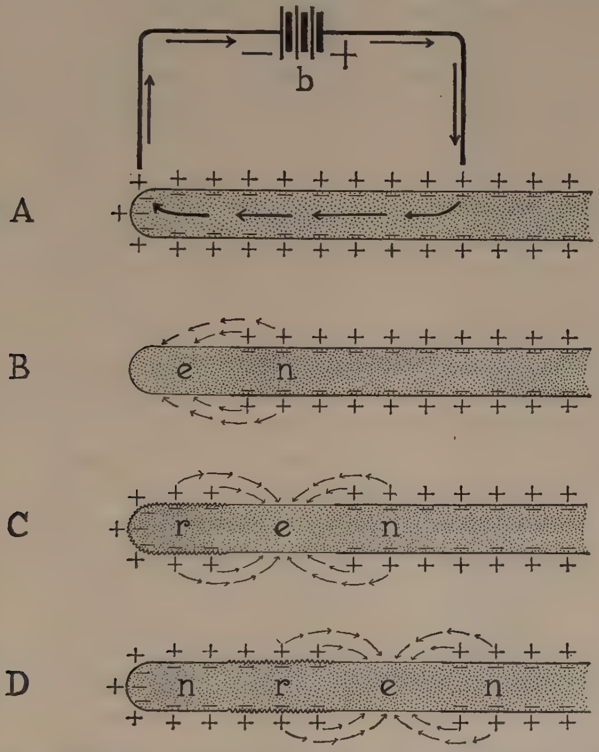


FIG. 100.—Diagrams illustrating the theory of transmission of excitation. *A*, a resting (unexcited) nerve fiber; its surface membrane is electrically polarized, as indicated by the signs; an artificial electric current is passed through the nerve, in the direction shown. *B*, the nerve fiber becomes excited at the point of application of the negative electrode, where its normal polarization is abolished. *C*, *D*, transmission of the state of excitation along the fiber. *b*, battery; *n*, normal (unexcited) region of the nerve fiber; *e*, excited region; *r*, refractory region; heavy arrows indicate direction of the stimulating current, light arrows direction of the action current.

than in any other tissue; in the motor nerves of mammals it attains a velocity of 120 meters per second (at body temperature).

It has recently been demonstrated that the nerve-impulse produces, in addition to the action current, a minute but measurable amount of heat, and also consumes oxygen and liberates CO_2. These facts indicate a metabolic process of the oxidative type. Most—at least 90%—of the heat production, and probably all of the oxygen consumption and CO_2 liberation, occur *after* the passage of the state of excitation, indicating that the oxidative reactions are involved in the *recovery process*, or restoration of the resting condition, rather than in the excitation process itself, just as in muscle (p. 268). We know as yet very little about the actual chemical reactions involved in nerve action; they may or may not be the same as those in muscle. At any rate, the amount of fuel substance (*e.g.*, carbohydrate) consumed in nervous activity is very minute, even in comparison with the size of the nerve fiber. The amount of heat produced by a stimulated nerve is equal to that which would be liberated by the oxidation of 0.000001 gram of glycogen (or its fragmentation products) per gram of nerve per minute. Thus, if the nerve contains 1% of fuel substance, it could be stimulated continuously for a week without exhaustion. It is found, in fact, that nerve fibers are practically unfatigable provided the oxygen supply is adequate. Small as is the amount of heat produced by the nerve-impulse, it represents about a thousand times as much energy as the action current does; there seems no doubt, therefore, that the energy of the nerve-impulse is afforded by the chemical reactions occurring in the fiber itself as the impulse travels along it. If this be true, we should expect that the strength of the nerve-impulse at any point would depend solely on the local condition of the nerve fiber, not on the nature or magnitude of the stimulus arousing it. This is found, in fact, to be true; *i.e.*, each individual nerve fiber acts according to the all-or-none law (p. 243).

Many factors—*e.g.*, temperature, oxygen supply, the concentrations of various ions or other chemical substances—may affect the excitability of the nerve fiber. Among the most important of these factors are the effects of previous excitation. As we have already learned (p. 241), the state of excitation in a nerve (or any other tissue) is always followed by a period during which the nerve is absolutely incapable of excitation by any stimulus, however strong: this is called the *absolute refractory period.* The absolute refractory period is followed by a longer *relative refractory period,* during which the excitability of the nerve gradually returns to normal: during this time, it requires a stronger stimulus than normally to excite the nerve, and the magnitude of the nerve-impulse thus aroused is less than normal. The relative refractory period is followed, in turn, by a *supernormal period,* during which the nerve can be excited by a weaker stimulus than normally, and the magnitude of the nerve-impulse is greater than normal (Fig. 101). The duration of these three periods (in the sciatic nerve of the frog) is approximately:

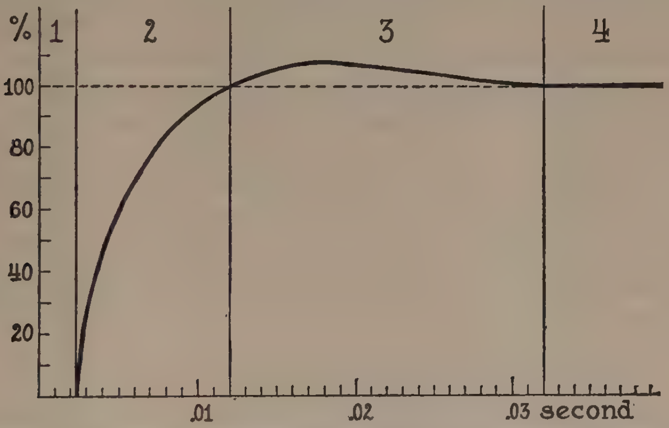


FIG. 101.—Variation of excitability of a nerve after stimulation. Abscissae: time after first stimulation. Ordinates: excitability, expressed as percent of normal excitability. *1,* absolute refractory period; *2,* relative refractory period; *3,* supernormal period; *4,* normal condition. (Adapted from Keith Lucas.)

absolute refractory period	0.002 second
relative refractory period	0.01 second
supernormal period	0.02 second

These periods may vary considerably, however, among different nerves, or even perhaps among the individual fibers. These time-variations in susceptibility to successive stimuli, and in magnitude of the resulting impulses, are believed to play an important rôle in the complex phenomena of the central nervous system of higher animals (p. 304).

Neuroid transmission.—The transmission of the state of excitation seems to be a general property of all living protoplasm. We have already seen, in the previous chapters, various examples of transmission of excitation in organisms without nerves and in non-nervous tissues. This is sometimes called *neuroid* transmission, to distinguish it from true nervous conduction, but the mechanism is, in all probability, essentially the same in both cases.

Among plants, transmission of the neuroid type is involved in the growth responses to gravity, light, etc., where the conductors of excitation are the undifferentiated parenchyma cells of the growing regions (p. 247). In some of the more specialized responses of plants, transmission is effected more rapidly by the sieve-tubes of the phloem, whose structure is somewhat comparable to that of nerves—long continuous strands of protoplasm not interrupted by transverse membranes (p. 167).

In unicellular organisms, neuroid transmission must be involved in all cases where the effective (*e.g.*, mechanical) response occurs at a different point than the incidence of the external stimulus (p. 244). This type of coordination is strikingly exemplified in the ciliates (*e.g.*, Paramecium), where the cilia beat in regular succession from front to rear. As previously mentioned, there seem to be, in some ciliates at least, visibly differentiated intracellular fibrils specialized for the conduction of excitation.

There are also many examples of neuroid transmission in multicellular animals. In the sponges, where there are no nerve cells at all, excitation is transmitted, rather slowly, through the ordinary epithelial or epithelio-muscular cells. The same mode of conduction may also occur in Hydra (and other coelenterates), especially in those regions where the nerve-net is not well developed. In higher animals, neuroid transmission is exemplified in all ciliary movements, which are apparently never under control of the nervous system. This type of transmission is also shown by visceral and especially by cardiac muscle, where the wave of excitation, manifested by both the electrical and the mechanical response, travels throughout the tissue even in the absence of nerve fibers. In the vertebrate heart, there are bundles of specially differentiated muscle fibers, connecting the auricles with the ventricles, whose sole function is conduction of excitation from the former to the latter.

All these cases of neuroid transmission are examples of nervous coordination, in the broad sense. This type of coordinating mechanism reaches its highest degree of efficiency, however, in the specialized *nerve tissues* found, in some form, in almost all multicellular animals.

The nerve-net.—The simplest type of true nervous system is found in Hydra and related animals (p. 249). It consists of a network of nerve fibers, lying among the bases of the epithelio-muscle cells of both cell layers. These nerve fibers are processes of two types of cells: the sensory cells and the nerve cells proper, often called *protoneurones.* The nerve-net extends throughout the body of the animal in a diffuse form; *i.e.*, nerve cells, with nuclei, as well as nerve fibers, are present in all parts of the body. There is believed to be direct protoplasmic continuity, without intervening cell membranes, throughout the net; *i.e.*, the nerve-net is essentially an extensive syncytium with larger aggregates of protoplasm, containing nuclei, at the nodes of the network. Between the nerve fibers and the muscle processes there is probably not protoplasmic continuity, but merely close contact.

A state of excitation aroused by a stimulus at any point of the organism tends to be transmitted rapidly in all directions throughout the nerve-net. This transmission is, however, somewhat limited in direction and extent by several factors. One of these is the direction of the nerve fibers: in the tentacles, for instance, these fibers run chiefly from the sensory cells toward the *base* of the tentacle; thus, when any point of the tentacle is stimulated, the response is chiefly from this point toward the base. Another factor modifying conduction is the effects of previous excitation; *i.e.*, the refractory state, etc. (p. 297). It has been shown experimentally in animals (jellyfish) with a nerve-net that the conduction of excitation is limited by the refractory state of those parts of the net just previously excited. Mechanical factors may also modify its excitability: thus, the nerve-net must be stretched in those regions where the body is extended, and vice versa; and it seems that a stretched portion of the net is more irritable (*i.e.*, more easily excited) than a more contracted portion. At the myo-neural junctions between nerve fibers and muscle processes, the peculiarities of conduction across a synaptic membrane (which will be described presently) probably also come into play. By the interaction of all these, and perhaps other, factors, the nerve-net serves as a mechanism not merely for general and indiscriminate conduction but for the coordination of fairly complex movements.

Although the main portions of the nervous system of higher animals have a quite different structure, nerve-nets essentially similar to that of Hydra are found in certain internal organs of these animals. The nerve plexuses of the enteron, and perhaps of some other organs, in vertebrates seem to be of this type. To what extent these net-like nerve plexuses are independent of the central nervous system is still an undecided question.

The synaptic nervous system.—The nervous system of practically all animals above the coelenterates differs from the nerve-net in two significant respects. In the first place, the cell-bodies, containing the nuclei, of almost all the nerve cells (except, in many cases, the sensory neurones), instead of being scattered through the animal, are aggregated into compact *ganglia*, the largest of which make up the *central nervous system*, from which the nerves, consisting of fibers only, ramify throughout the body. Almost all nerve-impulses, on their way from receptors to effectors, pass through the central nervous system, which thus acts as a central organ for the coordination of all the activities of the animal.

A still more important difference is in the nature of the junction between individual nerve cells. In most parts of the nervous system of the higher animals there is not protoplasmic continuity from cell to cell, as in the nerve-net, but merely close contact. Throughout all the parts of one neurone—cell-body, dendrites, axon and its branches—there is direct protoplasmic continuity, but at the points where the terminal branches of the axon of one neurone make contact with the dendrites of another neurone (p. 254), this continuity is interrupted by a cell membrane separating the two cells. This point of contact is called a *synapse.* A similar junction exists at the point of contact of nerve fibers with muscle cells, the *myo-neural junction.* Many of the complex nervous phenomena of higher animals are explicable on the basis of certain peculiarities of these synaptic junctions in respect to irritability and transmission of the nerve impulse.

One-way conductivity: the "law of forward direction."—Within the limits of a single neurone, the state of excitation spreads equally in all directions from any point stimulated. But across the synapse it is transmitted in only one direction: *from* the axon of one cell *to* the dendrites of the other—never in the opposite direction. This peculiarity can be stated in another way: the "receptive" part of the cell—usually the dendrites—is more sensitive than the axon, so that the dendrites are stimulated by the action current of the contiguous axons, but the axons are not stimulated by that of the dendrites. The same is true of the myo-neural junction: excitation is transmitted from the axon (efferent nerve fiber) to the muscle cell, but not in the opposite direction. There is strong evidence of the existence of a special *receptive substance* in the muscle cell at its point of contact with the nerve fiber. Because of this *one-way conductivity* of the synaptic junctions, and the arrangement of the cells in the animal (p. 255), the nerve-impulse always travels, under normal conditions, from the sensory to the motor neurones and thence to the effectors—never in the opposite direction. This "*law of forward direction*" is one of the important differences between the synaptic type of nervous system and the nerve-net type, which transmits equally in all directions.

Synaptic block: localization and modifiability of response.—The nervous system, in all animals above the coelenterates, is made up of a large number of *reflex arcs*, each consisting of at least two neurones: a sensory neurone, whose axon (afferent nerve fiber) terminates within the central nervous system, and a motor neurone, whose dendrites and cell-body lie, in most cases, within the central nervous system (p. 255). The terminal branches of the afferent fiber may make synaptic contact directly with the dendrites of the motor neurone, or one or more intermediate neurones—lying, usually, entirely within the central nervous system—may be intercalated in the arc. Because of this structural arrangement and the law of forward direction, every nerve-impulse must pass through this series of neurones successively, before a stimulus in a receptor can elicit a response in an effector. The reflex arc may therefore be called the *functional unit* of the synaptic nervous system. The individual reflex arcs are, however, not structurally isolated from each other. Through the numerous branches of the axons and dendrites of the sensory, intermediate, and motor neurones, probably every neurone in the animal has synaptic contact, directly or indirectly, with every other neurone. Our general knowledge of the responses of higher animals, however, suffices to show that a nerve-impulse initiated at one point does not, normally, spread throughout the nervous system. One of the most characteristic features of the behavior of these animals is the *localization* of response; *i.e.*, stimulation of a single receptor or group of receptors usually elicits response in only a definite limited group of effectors. This indicates that, although there is *structural* contact throughout the whole nervous system, there must be some kind of *functional* obstruction to the transmission of nerve-impulses. Since we know that a state of excitation tends to spread throughout a single neurone—cell-body and all its fibers—with undiminished intensity from any point stimulated (p. 295), the synapses are indicated as the seat of this *block*. Various kinds of experimental evidence confirm this view of the function of the synapses. The time elapsing between the stimulation of a receptor (or a sensory neurone) and the response of the effector—the *reflex time*—is much greater than that required for the passage of the nerve-impulse through the length of nerve involved plus the latent period of the effector itself. The same is true when a muscle is stimulated through its motor nerve. The seat of this *delay* must be at the synapses—both in the central nervous system and at the myo-neural junction—and the delay is found, indeed, to increase with the number of synapses involved in the reflex arc. The time required for the nerve-impulse to traverse the very minute thickness of the synaptic junctions is therefore longer than for a much greater length of nerve fiber.

The tendency to block the nerve-impulse must vary from one synapse to another, affording definite *paths of least resistance* through the nervous system, resulting in definite localized responses. The conductivity of any one synapse is, however, by no means a fixed quantity, but may vary, in either direction, under different conditions. The irritability of the synapse, like that of nerve fibers and other tissues, may be increased or diminished by various factors, internal and external (p. 296). The synapses, however, seem to be much more susceptible than the nerve fibers to such effects. These variations in the conductivity of the synapses underlie the *modifiability* of response which renders the behavior of the higher animals so complex and largely unpredictable.

Certain drugs (*e.g.*, nicotine) diminish or entirely abolish the conductivity of synapses, thus diminishing or abolishing response and feeling; while other drugs (especially strychnine) have the opposite effect, increasing the conductivity of the synapses so that the slightest stimulus at any part of the animal elicits convulsive contractions of all the muscles of the body. The synapses are also extremely susceptible to deprivation of oxygen, losing their conductivity entirely after even a brief asphyxiation. All these effects are reversible if not too greatly prolonged.

The most important changes in the conductivity of synapses, from the viewpoint of normal behavior, are those resulting from the effects of previous stimuli. These effects can all be demonstrated in other tissues—nerve fibers, muscles, etc.—but in the synapses some of them are exaggerated or at least unusually conspicuous under normal conditions. Since stimuli can reach the synapses only by way of the nerve fibers, and these are incapable of transmitting excitation continuously (p. 297), the stimulation of the synapses is necessarily always intermittent. As in other tissues, the effect of repeated stimulation may be either to increase or to diminish irritability and the magnitude of the response, depending on the frequency and the duration of the intermittent stimulation.

Summation of stimuli.—It frequently happens that a single stimulus, applied to a receptor or afferent nerve fiber, may not evoke any apparent response, but the repetition of the same, or even a weaker, stimulus several times at sufficiently frequent intervals may do so. This means, apparently, that some synapse, which at first blocked the passage of the nerve-impulse, has had its irritability augmented by the successive stimuli until it finally transmits the wave of excitation to the effector. This phenomenon, called *summation* of stimuli, which is especially prominent in the central nervous system, is thought to be related to the supernormal phase of irritability in nerve fibers and other tissues (p. 297). It depends largely on the exact time interval between the successive stimuli as they reach the synapse. This interval, however, may depend not only on the frequency of the original (external) stimuli, but also on their strength and point of application, *i.e.*, on what nerve fibers transmit them. Therefore a synapse which may block completely the nerve-impulse aroused by one type of stimulation may transmit another readily; the two kinds of stimuli will thus elicit entirely different responses.

Inhibition.—Stimuli which reach the synapse at a greater frequency may have just the opposite effect; each successive stimulus may fall within the subnormal (relative refractory) phase of the synapse, and thus diminish its irritability for following stimuli. Under this condition, the synapse may become impermeable for nerve-impulses which it would ordinarily transmit. We find very often, in fact, that the application of one stimulus may prevent the normal response to another stimulus applied simultaneously, or bring about the cessation of some activity already in progress. In many cases, indeed, the only apparent result of a stimulus is to *stop* some activity of the animal rather than to initiate one. This phenomenon, called *inhibition*, plays a very essential rôle in the coordinated responses of animals. It means, apparently, the blocking of some synapse in the course of the usual path of the nerve impulse. As indicated above, it may be explained as a prolonged refractory period, due to the too great frequency of the impulses arriving at the synapse.

Synaptic fatigue.—The prolonged repetition of stimuli, even of the right frequency for transmission, will always, sooner or later, result in a failure of response. This kind of block, due to *fatigue* of the synapses, can only be removed by a period of rest with an adequate supply of oxygen—just as in the case of fatigue of muscle cells (p. 268). The synapses in the central nervous system are more quickly fatigued than the myo-neural junctions, which, in turn, become fatigued much sooner than the muscle cells themselves; the nerve fibers, as we have seen (p. 296), are practically unfatigable under normal conditions.

Facilitation: modification of behavior by experience.—In addition to these relatively brief changes of conductivity which have been described, there are, at least in the higher animals, more enduring modifications of the neural pathways due to repeated stimulation. The passage of a succession of nerve-impulses along the same pathway has the effect of *increasing* the conductivity of this path for succeeding stimuli. This effect, called *facilitation*, increases with repetition of the stimulus up to a certain point; thereafter, further repetition produces no further change until fatigue begins. The facilitation effect, however, disappears only very slowly and gradually; it may, in fact, endure throughout the whole lifetime of the animal, producing permanent changes in the conductivity of its neural pathways and consequently in its responses to certain stimuli. This phenomenon, which lies at the basis of *learning*, *habit*, and *memory*, is believed to be due to a permanent or semi-permanent increase of conductivity in some synapses by their repeated excitation. This effect is slowly reversible; *i.e.*, a prolonged period of disuse of these particular pathways results in a gradual decrease of the synaptic conductivity toward its original value: the corresponding changes in behavior are called *forgetting* or *loss of habit*. These phenomena of *modification of behavior by experience*, which play so large a part in the responses of the higher vertebrates, especially man, will be discussed further in the following chapter.

Functions of the nerve cell-bodies.—It will be noted that, in discussing the activities of the nervous system, we have spoken only of the nerve fibers (axons and dendrites) and their points of contact, the synapses. What, then, are the functions of the cell-body (*centron*) of the neurone? This part of the nerve cell always contains the nucleus. Just as in any other type of cell, a part of the cell cut off from the nucleated portion may continue for some time to perform normally those functions involving only *destructive* metabolism—including irritability and transmission of excitation—but eventually dies, owing to the failure of constructive metabolic processes which seem to be necessary for the prolonged maintenance of protoplasmic structure even in full-grown cells. Nerve fibers, cut off from their cell-bodies, may survive for several days, during which they transmit excitation perfectly normally. In most neurones (bipolar and multipolar types), the nerve impulse necessarily traverses the cell-body in passing from dendrites to axon. But in some neurones (unipolar type, *e.g.*, most sensory neurones of vertebrates), the dendrite connects directly with the axon; in such cases, it has been shown that the destruction of the cell-bodies does not impair, for some time, the normal functioning of the reflex arcs. We are, therefore, probably justified in concluding that the centron and the nucleus play no *direct* rôle in the functional activities (excitation and conduction) of the neurone.

It was formerly supposed that the nerve cells of the central nervous system might initiate nerve-impulses in the absence of stimuli reaching them through afferent fibers. Casual observation of the behavior of higher animals, including ourselves, seems to indicate that many of their activities are "spontaneous," without immediate stimuli. Experimental study, however, fails to support this idea. An animal with all its afferent nerve fibers cut does absolutely nothing, even though the central nervous system, efferent fibers, and effectors remain perfectly intact and capable of normal functioning. The *rhythm* of discharge—*i.e.*, frequency of waves of excitation—of nerve cells may be modified by changes in the fluids surrounding them. This is an important factor in the normal functioning of the *respiratory center*—that part of the nervous system controlling the breathing movements—in vertebrates, which is affected in this way by minute changes in the concentration of H^+ and OH^- ions in the blood; and also of the *temperature-control center* of warm-blooded animals, which is affected by changes in the temperature of the blood flowing through it; but, even in these cases, the normal functioning of these nerve centers depends chiefly on afferent impulses initiated by receptors. It is possible that nerve cells may possess some automatic activity—as, for instance, cardiac muscle cells do (p. 263)—but this is certainly not a prominent feature of the nervous system. We must regard the nervous system as essentially a highly complex system of connections for the conduction of excitation from receptors to effectors. The paths of conduction, which determine the nature of the response to any particular stimulus, may be modified by changes within the central nervous system itself, as we have seen; but the most important of these modifications, under normal conditions, are those resulting from stimuli reaching the central neurones through afferent fibers as a result of stimulation of receptors.

Structure of the vertebrate central nervous system.—The central nervous system reaches its highest degree of structural and functional complexity in the vertebrates, culminating in man. The vertebrate central nervous system has the general form of a hollow tube, extending lengthwise on the dorsal side of the body. Throughout the greater part of its length, this tube of nerve tissue has a simple, approximately cylindrical, form; this part is called the *spinal cord*. At its anterior end, in the head, the neural tube is enlarged and variously modified, forming the *brain* (Fig. 102).

A cross-section of the spinal cord reveals two regions: an outer one, the *white matter*, composed entirely of axons, most of which run lengthwise in the cord; and an inner region, the *gray matter*, composed chiefly of nerve cell-bodies and their dendrites (Fig. 105). The axons of the white matter comprise: afferent fibers entering the cord from sensory neurones which lie outside it, most of which turn to run lengthwise through the white matter, all terminating finally in the gray matter of the cord or of the brain; axons of intermediate neurones in the gray matter of the cord, most of which turn to run lengthwise through the white matter and finally terminate in the gray matter of the cord or brain; axons of intermediate neurones in the brain, running posteriorly through the white matter of the cord and terminating in its gray matter; efferent fibers running transversely through the white matter from the

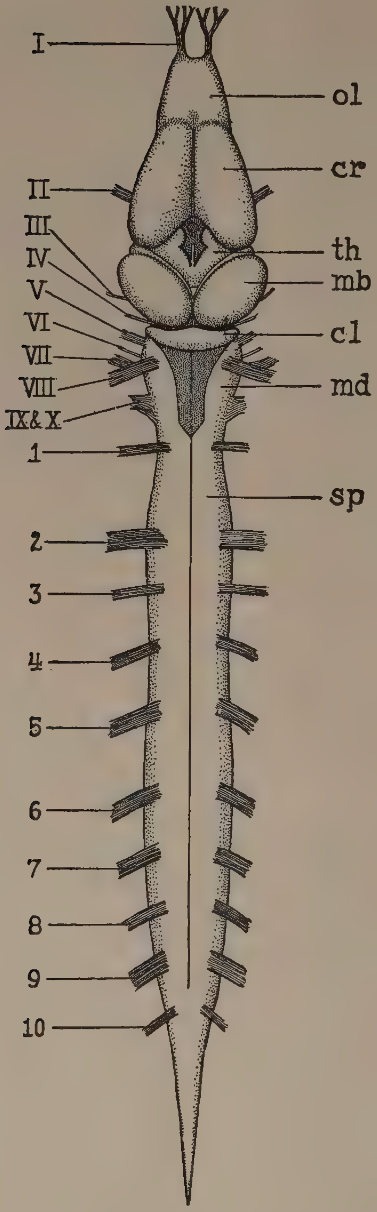

I
ol
cr
II
III
IV
V
VI
VII
VIII
IX & X
th
mb
cl
md
1
sp
2
3
4
5
6
7
8
9
10

FIG. 102.—Central nervous system of the frog, from the dorsal side. *ol*, olfactory lobe; *cr*, cerebrum; *th*, thalamus; *mb*, midbrain (optic lobe); *cl*, cerebellum; *md*, medulla; *sp*, spinal cord. *I–X*, roots of cranial nerves; *1–10*, dorsal roots of spinal nerves.

gray matter of the cord to the spinal nerves (Fig. 106). The white color of this region is due to the *myelin sheaths* which surround most of the axons. This sheath is composed of a glistening white fatty (lipin) substance, probably secreted by the axon; its function may be to insulate the fibers, so that the action current of one fiber does not stimulate other fibers lying alongside it. Some of the nerve cells in the gray matter are motor neurones, which send efferent fibers out through the spinal nerves to the skeletal muscles; the great majority, however, are intermediate neurones, most of which send axons out into the white matter, though some lie entirely within the gray matter. The cell-bodies and dendrites have no myelin sheaths; those axons and portions of axons lying within the gray matter are also usually non-myelinated.

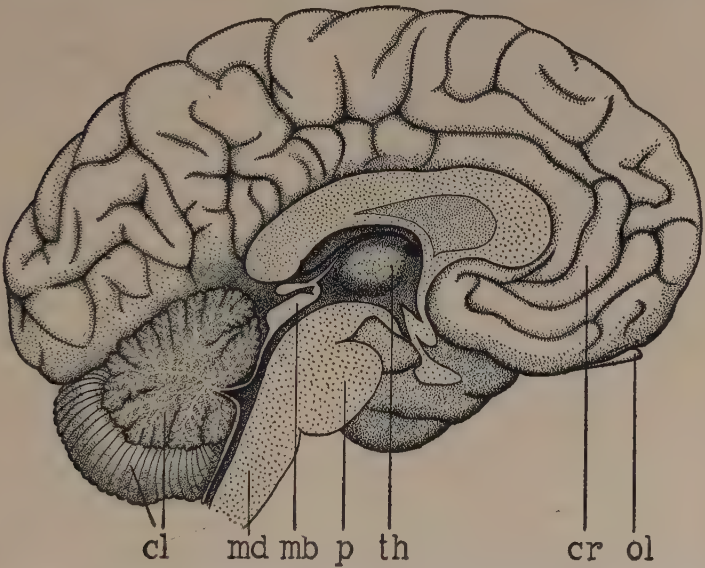


FIG. 103.—Median longitudinal section of human brain. *ol*, olfactory lobe; *cr*, cerebrum; *th*, thalamus; *mb*, midbrain; *p*, pons; *cl*, cerebellum; *md*, medulla.

Part of the brain has very much the same structure and cellular composition as the spinal cord; this part, called the *brain stem*, is essentially a forward prolongation of the spinal cord. The *higher nerve centers* are essentially expansions of the walls of certain parts of the brain. The most prominent of these, in most vertebrates, are the *cerebrum* in the anterior part, and the *cerebellum* in the posterior part, of the brain. These structures increase in size and complexity from the lower to the higher vertebrates, until in man they—especially the cerebrum—overgrow and conceal (from the dorsal and lateral aspects) all other parts of the brain (Fig. 103). In these parts of the brain there is an extensive layer of gray matter, the *cortex*, outside the white matter. The cortex consists entirely of intermediate neurones, most of which lie entirely within the cortex; others send axons through the underlying white matter to other parts of the cortex or down to the brain stem and the spinal cord (Fig. 106). This white matter also contains axons of cells in the brain stem or the cord running *to* the cortex.

Peripheral ganglia are masses of nerve cell-bodies lying outside the central nervous system. These are of two kinds: *sensory* and *motor* ganglia. The sensory ganglia contain the cell-bodies of practically all the sensory neurones of the vertebrate body, except those which lie in the sense organs themselves (nose and eye); the central nervous system contains no sensory neurones (with a few possible exceptions in the brain stem). Most of these sensory ganglia lie close to the cord or brain stem; their neurones are mostly unipolar cells, sending out a single fiber which divides into two branches, one running out to a receptor, the other in to the central nervous system (Fig. 105).

The motor ganglia outside the central nervous system, called *autonomic* ganglia, contain the cell-bodies of all the motor neurones innervating the involuntary (smooth and cardiac) muscles and the glands. The autonomic ganglia are divided into two groups: the *sympathetic* ganglia, lying close to the spinal cord or in the abdominal cavity; and the *parasympathetic*, lying in or close to the organs they innervate (Fig. 104). Many of the internal organs (heart, digestive organs, etc.) receive efferent fibers from both sympathetic and parasympathetic neurones. In these cases, the two have antagonistic effects: *e.g.*, stimulation of the sympathetic accelerates the heart beat, while that of the parasympathetic retards or stops it; in most of the digestive organs the effects are just opposite, parasympathetic stimu-

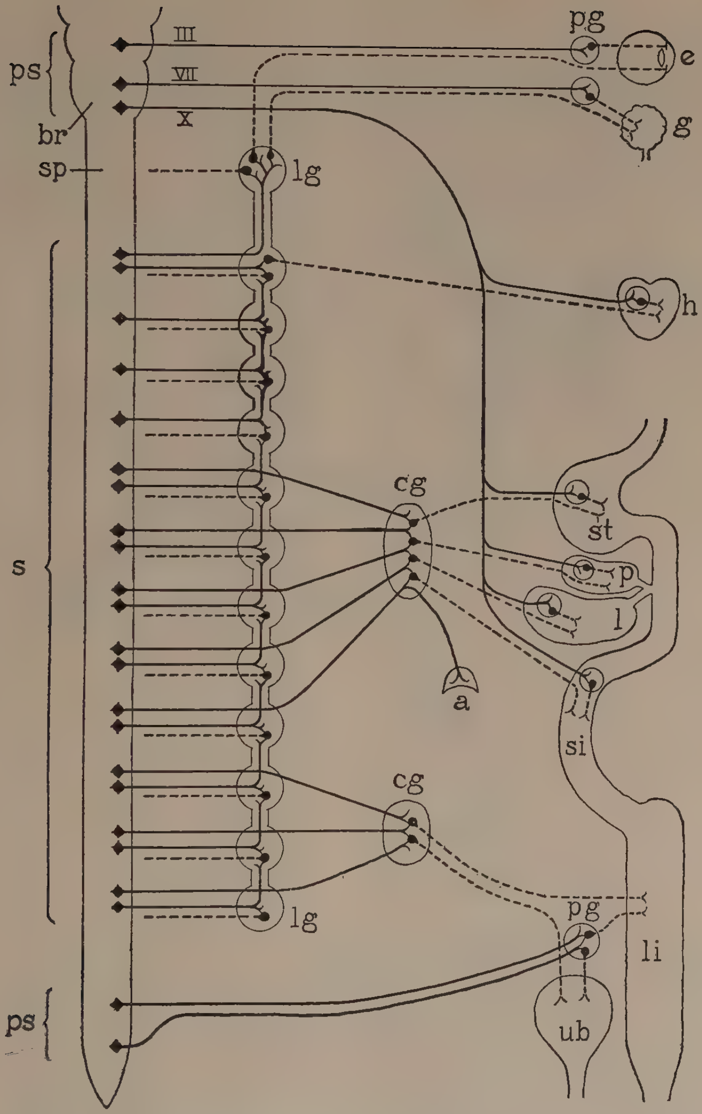


FIG. 104.—Diagram showing the distribution and connections of the autonomic nervous system. The heavy lines represent pre-ganglionic fibers, the dotted lines post-ganglionic fibers. *s*, sympathetic system; *ps*, parasympathetic system; *br*, brain; *sp*, spinal cord; *lg*, lateral sympathetic ganglia; *cg*, collateral sympathetic ganglia; *pg* (and also the ganglia within the visceral organs), parasympathetic ganglia; *e*, eye; *g*, salivary gland; *h*, heart; *st*, stomach; *p*, pancreas; *l*, liver; *a*, adrenal gland; *si*, small intestine; *li*, large intestine; *ub*, urinary bladder; *III*, *VII*, *X*, cranial nerves (*X* is the vagus nerve). The post-ganglionic fibers shown running back toward the spinal cord run in the spinal nerves to the sweat glands, hairs, and blood vessels of the body wall (see Fig. 105).

lation arousing muscular contraction, sympathetic stimulation inhibiting it. Some of these organs (notably the enteron) also have nerve-net-like structures in their walls; whether these are connected with the autonomic system or entirely independent is not yet certain. The smooth

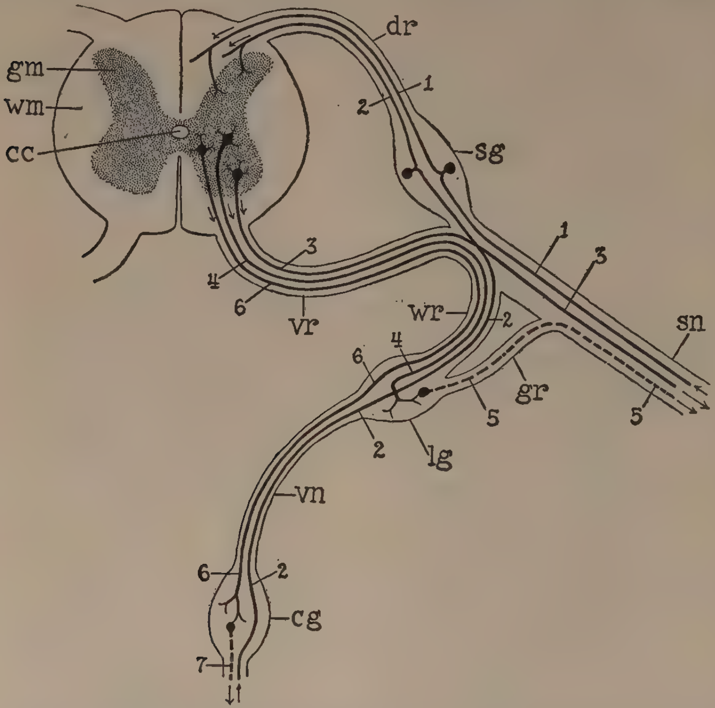


FIG. 105.—Diagram showing cross-section of the spinal cord and relations of the spinal nerve and sympathetic ganglia on one side. *gm*, gray matter of the cord; *wm*, white matter; *cc*, central canal; *dr*, dorsal root of spinal nerve; *sg*, sensory ganglion; *vr*, ventral root; *sn*, spinal nerve; *wr*, white ramus; *gr*, gray ramus; *lg*, lateral sympathetic ganglion; *vn*, visceral nerve; *cg*, collateral sympathetic ganglion. *1*, afferent nerve fiber from receptor in skin or body wall; *2*, afferent nerve fiber from receptor in viscera; *3*, efferent nerve fiber to skeletal muscle; *4*, pre-ganglionic fiber to lateral ganglion; *5*, post-ganglionic fiber to smooth muscle or gland of skin or body wall; *6*, pre-ganglionic fiber to collateral ganglion; *7*, post-ganglionic fiber to viscera. Arrows indicate directions of the nerve-impulses in the fibers.

muscles and glands of the body wall (skin muscles, peripheral blood vessels, and sweat glands) have only sympathetic innervation.

Nerves.—The central nervous system and the peripheral ganglia are connected with each other and with all parts of the body by *nerves*—bundles of axon fibers, mostly myelinated. The *spinal nerves* arise from the sides of the spinal cord, in pairs (*i.e.*, in corresponding positions on the two sides). The number of pairs of spinal nerves differs greatly in different vertebrates; *e.g.*, there are only 10 pairs in the frog, 31 pairs in man, and much larger numbers in some of the lower vertebrates, especially fishes. Each spinal nerve arises from the cord by two *roots*. The *dorsal root* contains only *afferent*, the *ventral root* only *efferent*, nerve fibers. Each dorsal root, close to its emergence from the cord, enters a sensory ganglion, which contains the cell-bodies of all the neurones whose fibers compose the dorsal root. The ventral root consists of axons whose cell-bodies lie in the gray matter of the cord. Shortly beyond the sensory ganglion (dorsal root ganglion), the two roots unite. From this point on, the nerve consists of both afferent and efferent fibers; each nerve contains some thousands of these nerve fibers. The nerve branches repeatedly, sending branches to many parts of the body; but the individual fibers do not branch until they reach their terminations in receptors or effectors. Many of the fibers of the ventral root are axons of motor neurones in the cord, which run directly to skeletal muscles; but others are axons of intermediate neurones in the cord, which run to the sympathetic ganglia. These *pre-ganglionic fibers* make synaptic contact, in the sympathetic ganglia, with the dendrites of the sympathetic neurones, whose axons—*post-ganglionic fibers*—run out, as previously explained, to the involuntary muscles and the glands. Many of the post-ganglionic fibers turn back into the spinal nerves and run in these to their destinations; some, however, form separate nerves running to the internal organs. The post-ganglionic fibers are non-myelinated; the pre-ganglionic, and most of the other fibers in nerves, are myelinated. The parasympathetic ganglia of the posterior part of the body (large intestine, excretory and reproductive organs) receive pre-ganglionic fibers from the posterior end of the spinal cord. The autonomic neurones are, normally, excited only by stimuli reaching them from the central nervous system through the pre-ganglionic fibers. There are, however, more post-ganglionic than pre-ganglionic fibers; *i.e.*, each pre-ganglionic fiber connects with several autonomic neurones. Consequently, the effect of excitation of a single pre-ganglionic fiber is more widely diffused than in the case of other ventral root fibers. The responses of involuntary muscles and glands are, accordingly, less accurately localized than those of skeletal muscles. Afferent fibers from receptors in the internal organs often run in the same nerves as the autonomic fibers, but have no connections with the neurones of the autonomic system except indirectly through the central nervous system.

The *cranial nerves* arise from the brain—mostly from the sides of the brain stem—in pairs (Fig. 102). There are 10 pairs of cranial nerves in the lower vertebrates (fishes and amphibia), 12 pairs in the higher classes (reptiles, birds, and mammals). Some of the cranial nerves contain only afferent, others only efferent, fibers; some, like the spinal nerves, contain both kinds of fibers. Just as in the spinal nerves, the afferent fibers are axons of cells lying in the sensory ganglia outside the central nervous system, while the efferent fibers are axons of cells lying in the brain stem. Here also the efferent fibers are of two kinds: motor fibers to skeletal muscles, and pre-ganglionic fibers to autonomic ganglia. All the pre-ganglionic fibers of the cranial nerves run to parasympathetic ganglia; most of these pre-ganglionic fibers run in the *vagus nerves* (10th pair of cranial nerves), which innervate the viscera of the thorax and abdomen as far back as the end of the small intestine (Fig. 104).

Conduction paths in the nervous system.—From what we have learned of the structure and function of the nervous system, it is obvious that the response of an animal to any particular stimulus, or combination of stimuli, will depend on the path traversed by the nerve-impulse through the nervous system from receptors to effectors. The structural complexity of the nervous system, in the higher vertebrates especially, is almost inconceivably great: the numbers of sensory and motor neurones are in the millions, while the intermediate neurones number billions. The manifold interconnections of these through their fibers, together with the variations of synaptic conductivity at their points of contact, render the possibilities of complexity and variability of conduction paths—and consequently of response—practically infinite. It is, nevertheless, possible to trace

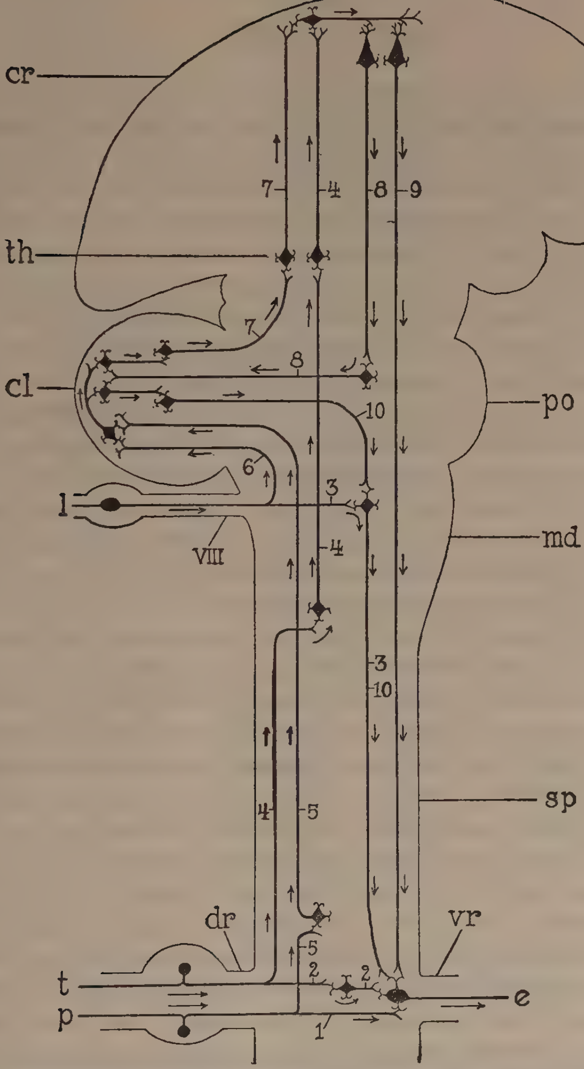


FIG. 106.—Diagram showing a few of the principal conduction paths within the central nervous system. *cr*, cerebrum; *th*, thalamus; *cl*, cerebellum; *po*, pons; *md*, medulla; *sp*, spinal cord; *VIII*, eighth cranial nerve (auditory-vestibular nerve); *dr*, dorsal root of spinal nerve; *vr*, ventral root of spinal nerve; *l*, afferent fiber from labyrinth; *t*, afferent fiber from tactile receptor; *p*, afferent fiber from proprioceptor; *e*, efferent fiber to skeletal muscle. *1*, simple two-neurone reflex arc; *2*, three-neurone intrasegmental reflex arc; *3*, intersegmental reflex arc; *4*, main afferent path from tactile receptors (and some other types of receptors) to cerebrum; *5*, main afferent path from proprioceptors to cerebellum; *6*, direct afferent path from labyrinth to cerebellum; *7*, path from cerebellum to cerebrum via thalamus; *8*, path from cerebrum to cerebellum via pons; *9*, main efferent path from cerebrum to skeletal muscles; *10*, efferent path from cerebellum to skeletal muscles. Arrows indicate directions of the nerve-impulses in the fibers. The interconnections of these paths, especially within the cerebrum and cerebellum, are actually much more complex than indicated in the diagram.

many of the main conduction paths through the nervous system, owing to the fact that many of the long axons in the white matter of the central nervous system form large bundles (*fiber tracts*) of fibers having similar origins and terminations. Practically every response involves a considerable number of receptor and effector cells, and consequently a number of neurone chains—reflex arcs—connecting these. The neural paths from a localized group of similar receptor cells to a localized group of effector cells usually run closely parallel; *i.e.*, through the same nerves, ganglia, and fiber tracts. At the same time, the various neurones in these paths have manifold connections with other neurones, so that the conduction paths may divide, unite, etc., in many complex ways. Thus a single stimulus may arouse a complex group of responses; and conversely, a number of simultaneous or successive stimuli may affect the response of a single effector organ.

The elucidation of conduction paths through the nervous system has been effected by the cooperation of several methods of investigation, *viz.: anatomical* methods, dissection and sectioning, revealing the course of fiber tracts and their relation to the ganglia of the gray matter; *experimental* methods, including localized stimulation of nerves, ganglia, and fiber tracts, extirpation of parts of the nervous system, cutting of fiber tracts with consequent degeneration of the severed axons, etc.; *clinical* methods, observation of functional abnormalities due to disease or accident and postmortem study of the corresponding nervous lesions.

Intrasegmental reflex arcs.—The simplest possible reflex arc involves two neurones: (1) a sensory neurone, whose axon makes direct contact with (2) a motor neurone in the gray matter of the cord or brain stem. Such two-neurone reflex arcs are believed to exist, in the higher vertebrates, only in the case of stimuli from the pressure receptors in muscles, tendons, and joints (p. 285). More usually, the reflex arc involves also one or more intermediate neurones between the sensory and the motor neurones. These intermediate neurones may be confined entirely to the gray matter, or their axons may run through the white matter to another part of the cord or brain stem, or out to an autonomic ganglion. In many two-neurone and some of the simpler three-neurone arcs, only one *segment* (the part giving rise to one pair of nerves) of the cord or brain stem is involved; *i.e.*, the impulse passes only through neurones lying entirely within one segment, and out through efferent fibers of the same nerve through whose afferent fibers it entered, or of the corresponding nerve on the other side. Such paths are called *intrasegmental reflex arcs*. The response, in such cases, is confined to the same part of the body as the original stimulus, or the corresponding part on the other side. Strictly intrasegmental reflexes may be common in such animals as the earthworm (p. 256) and perhaps some of the lower vertebrates, but they probably play relatively little part in the behavior of the higher vertebrates.

Intersegmental reflex arcs are those involving neurones in two or more segments of the spinal cord or brain stem or both, but not the higher centers. Impulses entering the central nervous system through the nerves of one segment may be transmitted to the motor neurones of other segments in several ways: through the afferent (sensory neurone) fibers themselves, most of which turn, after entering the central nervous system, and run longitudinally through the white matter; through the axons of intermediate neurones in the cord or brain stem, which also run longitudinally through the white matter to other segments; or through successive relays of short intermediate neurones lying entirely within the gray matter. Many of the long axons of the two types first mentioned run all the way from cord to brain stem, or vice versa, giving off side branches (*collaterals*) to many segments on the way. Thus an impulse entering the central nervous system through one nerve may stimulate motor neurones in many or all segments of the cord and brain stem. Conversely, a motor neurone in any part of the central nervous system may be stimulated *or inhibited* (p. 304), through its many-branched dendrites, by impulses from many parts of the nervous system. These intersegmental reflex arcs, involving only the spinal cord and brain stem, may thus mediate very complex responses. All such responses are, however, entirely unconscious and usually also quite invariable; *i.e.*, a particular *combination of stimuli* always evokes the same response; the effect of a single stimulus may, of course, be modified by those of other, simultaneous or briefly preceding, stimuli (p. 304).

Many of the muscular and glandular responses of internal organs—*visceral responses*—are of this nature. Stimuli from receptors located in these organs (p. 284) reach the central nervous system through afferent fibers of the spinal nerves and through afferent fibers running in the vagus nerves. Efferent impulses from the central nervous system reach these organs through the pre-ganglionic fibers of the vagus and spinal nerves by way of the autonomic ganglia. These various paths converge in the *medulla* (posterior part of the brain stem), where the vagus nerves arise and where the spinal cord joins the brain. In this region of the brain are found certain groups of intermediate neurones which act as coordinating *centers* for the various unconscious—but vitally important—activities; *e.g.*, the breathing movements, the heart-beat and regulation of blood-pressure, the control of body temperature (in warm-blooded animals), etc. These centers receive afferent impulses along the paths indicated above, and discharge efferent impulses to the autonomic ganglia, which stimulate or inhibit the involuntary muscles and glands. The activities of some of these centers may be modified by conditions in the blood surrounding them (p. 306); many of the visceral responses are also controlled in part by another kind of coordinating mechanism, as we shall see later (p. 321).

Suprasegmental paths are those involving the *higher centers* of the brain. These paths are essentially long reflex arcs, consisting of many neurones, including some in the cerebral or cerebellar cortex. Afferent impulses entering the spinal cord or brain stem may reach the cerebrum or cerebellum by many paths; *e.g.*, through afferent (sensory neurone) fibers running anteriorly through the white matter of the cord to the medulla, thence through intermediate neurones to the cerebellum or to the *thalamus* (anterior portion of the brain stem), whence a third relay of neurones carry the impulses to the cerebrum; through intermediate neurones of the cord whose axons run direct to cerebellum or thalamus; by shorter but essentially similar paths from the afferent nerve fibers of cranial nerves through intermediate neurones of the brain stem; by chains of short neurones through the gray matter of the cord and brain stem, etc. (Fig. 106). All these paths (with the partial exception of that from the labyrinth to the cerebellum) involve one or more intermediate neurones in the cord or brain stem. These intermediate neurones not only relay the afferent impulses to the higher centers, but also serve to "sort out" these impulses. Impulses from many kinds of receptors enter the central nervous system by the same nerve, but within the cord and brain stem the afferent fibers and those of the intermediate neurones are grouped according to the *kind of receptors* they connect with. Each fiber tract consists of fibers carrying nerve-impulses from the same kind of receptors, and therefore representing the same kind of original stimulus; thus, certain tracts carry impulses from tactile receptors, others from pain receptors, others from proprioceptors in the muscles and joints, etc. As we have previously seen (p. 283), the sensation aroused by any particular stimulus, as well as the response to the stimulus, depends on the connections of its afferent fibers within the central nervous system. Only those stimuli reaching the cerebral cortex arouse sensations, the nature of the sensation depending on the part of the cerebrum stimulated, which, in turn, depends on the particular neural path through the central nervous system from sensory neurone to cerebral cortex.

Within the cortex of cerebrum and cerebellum the neural paths are impossible to trace. The cerebellar cortex contains about 1,000,000,000 neurones, and the cerebral cortex almost 10,000,000,000. Most of these lie entirely within the cortex. We have no idea through how many of these cortical neurones an impulse may pass successively. These neurones, also, have profusely branched fibers, so that one neurone may connect directly with hundreds or thousands of others; thus an impulse may spread more or less widely through the cortex, and, conversely, many impulses may converge to one point. Other cortical neurones send axons through the underlying white matter to other parts of the cortex: *e.g.*, from one part of the cerebrum to another; from one part of the cerebellum to another; or from cerebrum to cerebellum, or vice versa, by way of relays in the brain stem.

The cerebral cortex is involved in all conscious, or voluntary, activities. In this region occur those enduring modifications of synaptic conductivity which we call learning, habit, or memory (p. 305). Because of the practically infinite number of structurally possible pathways through the cortex, and their functional modifications by the effects of stimuli traversing them, the responses involving these cerebral paths are extremely complex and variable, and hence largely unpredictable. The chief path of nerve-impulses *from* the cerebrum to effectors is, in mammals, by way of certain large cortical neurones whose axons extend directly from the cortex to the motor neurones in all parts of the spinal cord and brain stem. In the lower vertebrates the chief path is more indirect, involving an additional relay of intermediate neurones in the brain stem. The direct path increases in relative size and importance from the lower to the higher mammals, thus bringing the motor neurones, and consequently the voluntary (skeletal) muscles which they innervate, more under the control of the cerebrum. This control consists not only in transmitting to the motor neurones stimulating impulses which would not otherwise reach them, but also—and very largely—in *inhibiting* their responses to stimuli reaching them from other parts of the nervous system. Thus the *intelligent* activities of higher animals are characterized not only by what they *do*, but also—and perhaps especially—by what they *don't do.*

The cerebellum is the central station for afferent stimuli from all the *proprioceptors—i.e.*, the pressure receptors in muscles, tendons, and joints, and those of the labyrinth (p. 285)—and the coordinating center for the delicate muscular responses involved in posture, locomotion, and other complex muscular activities. The paths of afferent impulses from these receptors to the cerebellar cortex have been indicated above. *From* the cerebellum impulses are carried by the axons of some of its cortical neurones, through one or more relays of intermediate neurones in the brain stem, to the motor neurones of the cord and brain stem, which are thereby stimulated or inhibited. There are, moreover, as previously indicated, paths from cerebellum to cerebrum, and vice versa, so that the activities of these two centers are closely correlated in the control of voluntary movements.

From the preceding discussion of conduction paths in the nervous system, it is apparent that a single sensory and a single motor neurone may be parts of many different functional paths; *e.g.*, a simple two-neurone arc, a three-neurone intrasegmental arc, intersegmental arcs including intermediate neurones in various parts of the cord and brain stem, suprasegmental paths involving the cerebellum or the cerebrum or both. Also, the millions of sensory and of motor neurones in the body may be connected, by way of these various paths, in practically any combination. It is impossible to trace, in detail, the neurone chains comprising the more complex paths including the cortex of cerebrum or cerebellum; but the visible structural complexity of these tissues, together with their known possibilities of functional modification (pp. 301–305) seem more than amply sufficient to account for the complex behavior of higher animals, including the mental activities of man. Probably not more than a small fraction of the possible neural paths, especially those of the cerebral cortex, are ever actually utilized by any one individual in a lifetime.

Chemical coordination.—The activities of different parts of an organism may affect each other through the agency of substances produced in one part and reaching other parts by diffusion or by circulation in the body-fluids (blood, lymph, etc.). This kind of interrelation is called *chemical coordination*, in distinction from the nervous type of coordination by transmission of excitation. Many of the waste products and intermediate metabolic products of cells may profoundly affect the metabolism and irritability of other cells; in this sense, chemical coordination is probably a very general phenomenon among organisms. There are also, at least in the higher animals, special substances, produced and secreted by particular organs, which have very specific effects on the metabolism and responses of other organs. These special agents of chemical coordination are called *hormones*. They are secreted, not to the outside of the body or into special cavities (*e.g.*, the enteron) by way of ducts, like other secretions, but directly into the body-fluids: this process is called *internal secretion*. Some hormones are produced by organs having also other functions; but some are produced by special organs, called *endocrine organs* or *ductless glands*, which have apparently no other function.

Hormones have been studied extensively, as yet, only in the vertebrates; but there is some evidence, as we shall see below, for the existence of some of these substances in lower animals and in plants also. Because of the striking pathological effects produced in the higher animals, including man, by excess or deficiency of certain hormones, the subject has attracted a great deal of attention in recent years. The amount of soundly established knowledge is, however, as yet very small in comparison with the mass of speculation —often wildly fantastic—in this field. We shall mention here only a few of the outstanding facts which seem to be most probably established.

We may, for convenience, divide the hormones roughly into three groups, according to their effects:

(1) hormones arousing specific responses (movement or secretion) in particular organs or tissues: *secretin*, *adrenalin*, and *pituitrin*.

(2) hormones affecting the general metabolic processes of the body: *insulin*, *thyroxin*, and the *parathyroid hormone*.

(3) hormones exerting specific effects on growth and development: *thyroxin*, the *anterior pituitary hormone*, the *sex hormones*, and the somewhat doubtful hormones of the *thymus* and *pineal* glands and the *adrenal cortex*.

These groups are by no means sharply defined, both because of the impossibility of drawing sharp distinctions between these three kinds of cellular activities, and because some hormones (*e.g.*, thyroxin) show more than one of these effects.

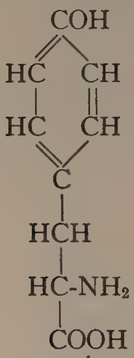
Secretin is the most striking example of a hormone arousing a specific localized response. This substance is produced and secreted into the blood by cells of the mucous membrane of the small intestine. It stimulates the pancreas, which it reaches by way of the blood stream, causing the secretion of pancreatic juice; it probably has a similar effect also on the liver and on the digestive glands of the intestine itself. Secretin is not secreted into the blood continuously, but only when *acid* is present in the cavity of the intestine. The food entering the intestine from the stomach is strongly acid (due to the HCl in the gastric juice); its entry therefore causes the liberation of secretin, which stimulates the pancreas, and probably the liver and intestinal glands, to secrete their digestive juices into the intestine. By this mechanism, the activity of these important digestive glands is aroused at the right time for their digestive function. These glands may also be partly controlled by a nervous mechanism, through the autonomic system, but the chemical mechanism is the more important one under normal conditions.

Secretin can be extracted from the intestinal mucosa artificially, by grinding it up in acid, and injected into the blood of another animal, producing its characteristic effects. Its chemical constitution is still unknown.

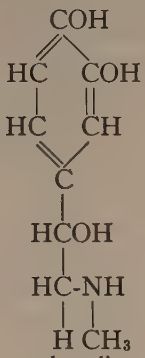
Adrenalin is an internal secretion produced by certain cells called *chromaphil cells*, which in the higher vertebrates form part of the *adrenal glands*, located near the kidneys. Adrenalin affects all those organs innervated by sympathetic neurones (p. 310), producing, in each case, the same effect—excitation or inhibition—as stimulation of the sympathetic nerve fibers; *e.g.*, constriction of blood-vessels, augmentation of the heart-beat, inhibition of the enteral muscles, discharge of glucose from the liver, erection of hairs, etc. These effects of adrenalin are produced even when the post-ganglionic fibers have all been cut; *i.e.*, it acts on the effector cells themselves—perhaps on the receptive substance at the myo-neural junctions (p. 305)—rather than through the nerve fibers. The chromaphil cells themselves, as shown by their development, seem to be modified sympathetic neurones; like these, they are innervated directly by pre-ganglionic fibers from the spinal cord (Fig. 104). Stimulation of the sympathetic pre-ganglionic fibers may therefore produce its characteristic effects in two ways: by the direct transmission of nerve impulses to the effectors through the post-ganglionic fibers; and by the liberation of adrenalin which, circulating in the blood, produces similar effects. The secretion of adrenalin is increased especially in states of excitement—*e.g.*, fear, rage, or sexual excitement—and seems to be largely responsible for the responses characteristic of these *emotional* states.

In some of the lower vertebrates chromaphil cells are found in all the sympathetic ganglia, widely distributed through the body. In a number of invertebrates, also, are found cells which appear to be chromaphil cells and are believed to secrete adrenalin. It is supposed that this substance, in all these animals, may be concerned in the regulation of blood-pressure by stimulating contraction of the muscular walls of the blood-vessels.

Adrenalin has been isolated as a pure chemical compound, and also synthesized artificially. It is an amine (organic base), closely related to one of the amino-acids, *tyrosine*, from which it is presumably produced in the cells.



tyrosine



adrenalin

A number of other amines, natural and artificial, chemically related to adrenalin, produce more or less similar effects in the animal body.

Pituitrin is a name applied to the internal secretion of the *posterior lobe* of the *pituitary gland*. This gland is a small body located on the ventral side of the brain stem in all vertebrates. It has a double origin, its anterior lobe being derived from the roof of the mouth while the posterior lobe is derived from the nervous system. The two lobes also secrete different hormones. The secretion of the posterior lobe stimulates contraction of all smooth muscles, regardless of their innervation; its effect is therefore similar to that of adrenalin in some cases, antagonistic in others. It has recently been shown that the material called pituitrin (*i.e.*, the secretion of the posterior pituitary lobe) probably contains at least two distinct hormones.

Insulin is an internal secretion of the pancreas. The cells producing this hormone, called *islet cells*, are entirely distinct from those producing the external secretion of the pancreas (pancreatic juice). Insulin plays an essential rôle in the metabolism of carbohydrates. In the absence of this hormone, glucose is neither decomposed and oxidized nor converted into glycogen, but accumulates in the blood and is excreted in the urine. Insulin is apparently necessary—perhaps as a catalyst—for the conversion of ordinary glucose, as it exists in solution in the blood, into an "active" form, by some kind of intramolecular change. Insulin alone can not effect this change, which does not occur in the blood where both glucose and insulin are normally present; some enzyme present in the tissues (*e.g.*, muscle cells) is also necessary. Only this "active" form of glucose can be metabolized in the cells, either destructively (fragmented and oxidized) or constructively (synthesized to glycogen).

The absence or deficiency of insulin, due to degeneration of the islet cells, causes the disease called *diabetes*, characterized by failure of normal carbohydrate metabolism. Diabetes was practically incurable before the discovery of insulin. It is now treated by injection of insulin into the blood; the effects, however, are only temporary and the treatment must be continued indefinitely.

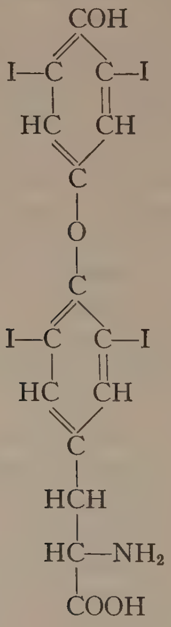
The chemical constitution of insulin is still unknown. It has some of the chemical properties of proteins, and is destroyed by pepsin or trypsin; for this reason it is entirely ineffective when taken by mouth. It seems to diffuse freely into and out of cells, however, and is therefore probably much simpler (*i.e.*, has smaller molecules) than the ordinary proteins.

The effects of insulin and of adrenalin on the blood sugar concentration are antagonistic: adrenalin increases the amount of glucose in the blood by stimulating the liver to discharge it, while insulin decreases it by accelerating its metabolism in the cells. Some other hormones—pituitrin and thyroxin—are also believed to affect the blood sugar concentration, but the mechanism of their effects is not yet clear.

Insulin or substances having very similar effects are found in many organisms, both animals and plants, including yeast. It is not improbable that all organisms may produce insulin or related substances playing a similar rôle in carbohydrate metabolism.

Thyroxin is produced and secreted into the blood by the *thyroid gland*, located in the throat region, below the pharynx, in all vertebrates. This hormone has a marked effect on the oxidative metabolism of the whole body. Absence or deficiency of thyroxin causes a marked decrease of the general oxidative metabolism, subnormal body temperature and pulse rate, excessive fat storage, physical and mental sluggishness. Excess of this hormone causes the opposite effects: high oxidative metabolism, body temperature, and pulse rate; emaciation and nervousness. Thyroxin also has striking effects on growth and development, which will be discussed later (p. 327).

Thyroxin has been isolated as a pure compound, and also synthesized artificially: its constitution is:



This shows it to be closely related to tyrosine (p. 324), from which it is presumably synthesized in the thyroid cells. Its most striking chemical characteristic is the fact that it contains a large proportion (about 65% by weight) of the element *iodine*. Deficiency of thyroxin in the organism may therefore be due either to deficiency of iodine in the food or to failure of the synthetic activity of the thyroid gland. In the former case, the deficiency can be corrected by feeding simple iodine compounds (inorganic iodides); in the latter case by feeding thyroxin or thyroid glands, which contain stored thyroxin.

The parathyroid hormone.—The *parathyroids* are four small glands, found in the higher vertebrates (amphibia and all higher classes at least), closely associated anatomically with the thyroid. These glands secrete into the blood a hormone which regulates some metabolic process or processes involving *calcium*, and controls the concentration of calcium salts in the blood. Deficiency of the parathyroid hormone causes a marked decrease of calcium ions in the blood, resulting in hyperirritability of the cells (p. 240), uncontrollable muscular spasms and convulsions. These symptoms may be relieved by the administration of calcium salts or of the parathyroid hormone. Excess of this hormone has the opposite effects: increase of calcium in the blood, resulting in apathy, drowsiness, and failure of the blood circulation. These symptoms may be relieved by the administration of sodium salts, which counteract the excess calcium (p. 240). Either excess or deficiency of the parathyroid hormone results fatally if uncorrected. The normal concentration of calcium ions in the blood depends on a balance between deposition and solution of calcium phosphate in the tissues, especially the bones. This balance appears to be controlled, in some as yet unknown way, by the parathyroid hormone, excess of the hormone favoring the solution, deficiency the deposition, of calcium phosphate. Insulin and, to a smaller extent, pituitrin are also said to increase the blood calcium concentration; the mechanism of these effects is still entirely unknown.

Hormones affecting growth and development.—A number of hormones produce striking effects on growth and development in vertebrates; practically nothing is yet known as to such effects in lower animals or in plants, although there has been much speculation on the subject.

Deficiency of *thyroxin* in children, or other young animals, produces—besides the effects mentioned above—

practically complete cessation of physical and mental development, resulting in dwarfism, idiocy, and sexual immaturity. Such individuals, when fed thyroxin or thyroid glands, begin to develop normally and continue to do so as long as this treatment is continued; the cures which have been effected in this way are very remarkable. The effects of thyroxin on development are especially striking in amphibia. The *metamorphosis* of the larval into the adult form (*e.g.*, of tadpoles into frogs) is dependent on thyroid secretion. If this gland is removed, metamorphosis does not occur, although the tadpole may continue to grow beyond its normal size. If thyroid glands or thyroxin be fed to such tadpoles, metamorphosis occurs promptly. The feeding of extra thyroid to very young normal tadpoles results in metamorphosis at a much earlier age and a much smaller size than normally. Certain species of salamanders which never undergo metamorphosis under natural conditions can be caused to do so by thyroid feeding. Amphibian metamorphosis may also be affected by some other hormones, as mentioned below.

The internal secretion of the *anterior lobe* of the *pituitary gland* has effects on growth and development somewhat similar to those of thyroxin, but affects particularly the growth of the bones. Deficiency of this hormone results in stunted growth, obesity, and sexual immaturity; excess of the hormone results in gigantism and especially excessive growth of bone. This hormone also affects amphibian metamorphosis in somewhat the same way as thyroxin.

The *gonads* (primary reproductive organs) are believed to produce internal secretions which influence growth and development. These *sex hormones* are supposed to be produced by certain cells, the *interstitial cells*, entirely distinct from those directly concerned in reproduction. The gonads affect growth and development in somewhat the same way as thyroxin, but particularly the development of the accessory reproductive organs and of the secondary sexual characters (differences between the two sexes not directly concerned in reproduction). Removal of the gonads in young animals results in failure to develop some of the normal characteristics of the proper sex, and, in some cases, development of some characteristics of the opposite sex. These results are ascribed to hormones produced by the interstitial cells which either stimulate development of the proper sexual characters or inhibit development of those of the opposite sex, or both. It has not yet been possible, however, to isolate hormones from the gonads which will produce these effects. In one case among invertebrates (crabs) it has been shown that such effects of the gonads are very probably due to their *removing* something from the blood rather than secreting something into it. In other invertebrates (*e.g.*, insects) the gonads have no effect whatever on the development of sexual differences in other parts of the body.

Many other effects have been ascribed to the sex hormones in vertebrates; *e.g.*, the failure of these secretions is supposed to play a large rôle in the symptoms of senility, etc. This whole subject, however, has been marked by such unscientific sensationalism and charlatanism that we must exercise extreme caution in accepting either the alleged facts or the proposed interpretations.

Several other endocrine organs in vertebrates are believed, on more or less convincing evidence, to affect growth and development. These effects are generally supposed to be due to hormones produced and secreted into the blood by these organs, but in none of the following cases have the effects yet been produced experimentally by substances extracted from the organs in question. The evidence is all based on the effects of removal or of abnormalities of these organs. In such cases, it is always possible that the organ produces these effects by *removing* something from the blood instead of by *adding* something to it. In either case such effects are examples of chemical coordination.

The *cortex* of the *adrenal glands*—which is quite distinct from the chromaphil tissue (p. 323)—is supposed to affect development in somewhat the same way as thyroxin, but particularly the development of the sexual organs. Deficient sexual development in adults is often associated with atrophy of the adrenal cortex, while precocious sexual development in children is often associated with hypertrophy of this tissue.

The *thymus gland* is an organ composed of lymphatic tissue (p. 198), located in the anterior part of the body cavity, near the thyroid, in all vertebrates. This gland is best developed in young animals and later declines and may even disappear entirely in the adult. Persistence of the thymus beyond its normal period is associated with sexual immaturity and retardation of development in other ways; so that it has been supposed that this gland produces a hormone inhibiting development. However, it has also been observed that the removal of the gonads of young animals results in persistence of the thymus gland, so that it is hard to say whether the persistence of the thymus in other cases is the cause or the result of the failure of normal development. Feeding thymus gland to tadpoles delays their metamorphosis into frogs, like removing the thyroid, so that the effects of these two glands seem to be antagonistic.

The *pineal gland* is a small body arising from the dorsal side of the brain stem in all vertebrates. Its history and supposed functions are similar to those of the thymus.

Many or all of these endocrine organs are supposed to exert profound effects on each other's development and functioning, but the evidence for most of these relations is conflicting and not yet conclusive.

Waste products as hormones.—Some substances which are primarily waste products of metabolism of cells may play important rôles in regulating the activities of certain organs; such substances are sometimes called *parahormones*. The most striking example of this kind is the effect of *carbon dioxide* on the *respiratory center* in the medulla (p. 318). The frequency of discharge of nerve-impulses by the neurones of this center, which stimulate the muscles involved in breathing movements, is determined largely by the concentration of CO_2 in the blood. The breathing movements are thus regulated in accordance with the needs of the animal; *i.e.*, a higher concentration of CO_2 results in faster breathing and increased ventilation of the lungs, and vice versa. It is not CO_2 directly which produces this effect on the neurones, however, but the H^+ ion concentration of the blood, which is, under normal conditions, determined largely by the CO_2 concentration (p. 228). Lactic acid, which may accumulate in the blood during severe muscular exercise, and other acids produced by abnormalities of metabolism, have similar effects.

In some of the lower vertebrates (sharks, etc.), *urea* seems to have some beneficial effect on the activity of the heart, as a certain concentration of this substance in the blood is necessary for maintenance of the normal heart beat. In the higher vertebrates it is not known to have any such effect.

General significance of chemical coordination.—The phenomena discussed in the preceding paragraphs suggest the possibility that many or all kinds of cells may discharge into the body-fluids substances—whether products of specific syntheses or incidental products of cell metabolism —which may regulate the activities of other parts of the organism. Plausible as this suggestion may seem, there is as yet no actual evidence to support it. In fact, as we have seen, almost all our present knowledge of coordination by internal secretions is confined to the vertebrate animals. Just as we have seen that coordination of the nervous type operates in plants and in unicellular animals, without specialized nerve cells, so it may be that chemical coordination operates in organisms without specialized endocrine tissues. One case suggesting this is the widespread occurrence of insulin, or insulin-like substances, in the lower animals and in plants, including at least one unicellular organism, yeast (p. 325). In the unicellular organism, at least, the substance must be produced in every cell; and this may also be true in some of the multicellular organisms.

We know that every cell produces, in its metabolic reactions, many substances which play essential rôles, as catalysts or otherwise, in subsequent processes within the same cell. These relations might quite logically be regarded as intracellular chemical coordination. From this point of view, the phenomenon of intercellular chemical coordination by means of specific internal secretions—hormones— in the higher animals is merely another example of the specialization and division of labor among cells which characterize the complex multicellular organism.

Interrelation of the chemical and nervous mechanisms.— In general, we may say that the various activities of an organism, whether unicellular or multicellular, are coordinated by two kinds of mechanisms: the transportation of actual substances from one part of the organism to another, and the transmission of a state of excitation. The latter mechanism is obviously more rapid and, at least in animals with a nervous system, capable of greater precision and complexity. In accordance with this, we find the external activities of organisms—such as those effected by the skeletal muscles of higher animals—controlled chiefly or entirely by the nervous mechanism, while the slower, more continuous and diffuse, internal activities involved in nutrition—digestion, circulation, respiration, metabolism, etc.—are controlled, in part at least, by the chemical mechanism. In the higher animals, each of these functions becomes largely localized in specialized tissues and organs—the nervous system and the endocrine organs, respectively. The two systems of control are, however, always closely interrelated, both by their simultaneous action on the same effectors and by their interaction on each other; *i.e.*, the endocrine glands may be stimulated through the nervous system, and the activities of the latter may be modified by hormones reaching it through the blood. Various examples of these types of interrelation have been mentioned in the preceding paragraphs.

STOP HERE

CHAPTER XVII

BEHAVIOR OF ORGANISMS

In the preceding chapters we have described some of the mechanisms by which the activities of organisms are effected and regulated. In the present chapter we shall discuss briefly the externally visible results of the operations of these mechanisms—the *behavior* of organisms under various external and internal conditions.

The behavior of organisms is commonly described under a number of rather vaguely defined terms, such as "reflexes," "instincts," "habit," "intelligence," etc. The chief theme of the present chapter will be to show that the various types of behavior designated by these words are all manifestations of the general responsiveness of living protoplasm to external and internal stimuli, manifested in various degrees of complexity in accordance with the structural and functional complexity of the special responsive mechanisms, especially those of coordination, in particular organisms.

Reflex action.—The term *reflex action* was originally applied to the type of response elicited by the stimulation of a single isolated *reflex arc:* receptor, afferent neurone, efferent neurone, and effector. In many such cases, the effector is located near the receptor—*e.g.*, a muscle lying immediately beneath a tactile receptor in the skin—so that the nerve-impulse seems to be "reflected" back from the central nervous system toward its point of origin, as light is reflected back toward its source by a mirror. This circumstance is the origin of the term "reflex"; the analogy to reflection of light is, however, entirely superficial and of no real significance. The effector responding to the stimulation of a given receptor may equally well be located in the opposite side, or in some even more distant part, of the body.

The real distinguishing feature of those responses commonly called reflex is that the response follows directly and in a generally invariable, predictable manner upon the application of a particular stimulus at a particular point. This simple type of behavior is especially characteristic of the lowest animals and of plants—organisms entirely devoid of a central nervous system and therefore of reflex arcs. The original meaning of the term reflex has therefore been extended to include all these cases of simple, direct responses to stimuli, regardless of the path of conduction of the state of excitation from receptor to effector.

The responses of plants to external stimuli are of this simple reflex type. A number of plant reflexes have been described previously (p. 245); *e.g.*, the drooping response of the Sensitive Plant (Mimosa), the curling of tendrils, the movements and secretion of insectivorous plants, the "sleep" movements of leaves and flowers, etc. The more general growth movements of plants will be mentioned again below (p. 336).

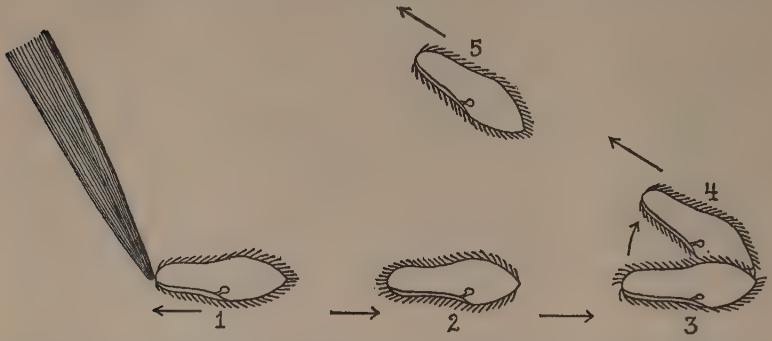


FIG. 107.—Motor reflex of Paramecium. *1*, position at moment of stimulation; *2*, *3*, *4*, *5*, successive positions thereafter; arrows indicate directions of movement. (Adapted from Jennings.)

The motor responses of protozoa are also simple reflexes, in the sense defined above. In Amoeba, the response to an external stimulus may be protrusion or retraction of one or more pseudopodia, depending on the nature, strength, and position of the stimulus. In more highly organized protozoa, such as ciliates and flagellates, the motor reflexes are not only more rapid and somewhat more complex in form, but usually also more stereotyped than in Amoeba. Paramecium, for instance, when swimming, responds to almost any kind of stimulus, whatever its nature or location, by reversing the effective stroke of its cilia (p. 271), swimming backward a short distance, then making a sharp turn toward its aboral side and swimming forward again (Fig. 107). Even small pieces of this organism respond in much the same way. Many other free-swimming ciliates and flagellates show motor reflexes of much the same form. In other ciliates, especially attached forms (*e.g.*, Vorticella), the motor reflex takes the form of a sudden contraction of the body and stalk, effected by the contractile myonemes (p. 244).

In the coelenterates (Hydra and its relatives), many stimuli elicit only simple reflex movements of the part directly stimulated; *e.g.*, contraction of a tentacle. Because of the presence in these animals of an extensive coordinating mechanism, however, certain stimuli may call forth complex coordinated movements of many parts of the body: tentacles, mouth, stalk, etc. Such responses represent combinations of simple reflexes, either simultaneous or successive. In this group of animals, however, because of the primitive structure of their nervous systems, these compound reflexes never attain the degree of complexity and precision which characterize the movements of animals with synaptic nervous systems.

In even the highest animals, many stimuli elicit simple reflexes, involving only one part of the body: examples of such simple reflex actions in ourselves are blinking, sneezing, coughing, swallowing, jerking back from a painful stimulus, etc. In the vertebrates, at least, it is found that the typical reflex responses to particular stimuli occur more certainly and uniformly after the brain has been destroyed or separated from the rest of the nervous system. These facts indicate that the higher nerve centers of the brain often inhibit or modify the local activities of the simpler reflex arcs of the spinal cord (p. 320). In most invertebrates, the "brain"—cerebral ganglia (p. 256)—seems to be much less important in this respect.

Tropisms.—One class of reflexes which has engaged a great deal of scientific attention, because they are especially susceptible to precise quantitative study, are those called *tropisms*. These are movements of growth, orientation, or locomotion, whose *direction* is determined by the direction from which the stimulus—*e.g.*, light, gravity, electric current, etc.—impinges on the organism. These responses are called, according to the nature of the stimulus directing them:

	Stimulus
phototropism	light
geotropism	gravity
galvanotropism	electric currents
chemotropism	diffusing chemical substances
stereotropism	contact with solid objects
etc.	

If the resulting movement is toward the source of stimulation, it is called a *positive* tropism; if away, a *negative* tropism; *e.g.*, a moth is positively phototropic, an earthworm negatively phototropic.

Tropisms were first studied in plants, in whose behavior, especially growth movements, they play an important and conspicuous rôle. It is very easy to demonstrate that the primary root of most plants is *positively geotropic* (Fig. 76), while the primary stem is *negatively geotropic*. The primary stem of most plants is also *positively phototropic*. The growing roots of plants are also "hydrotropic"; *i.e.*, they grow toward water. In the presence of excess water, the roots will grow away from the water; *e.g.*, to the surface of the soil. This, however, has been shown to be due, not to negative hydrotropism, but to positive "oxygenotropism." These are both special cases of *chemotropism*, *i.e.*, movements directed by the unequal concentration of some particular chemical substance on two sides of an organism. The stems and tendrils of many climbing plants exhibit *positive stereotropism; i.e.*, they grow toward any solid object with which they come in contact.

Many animals also show definite and precise tropistic responses to directive stimuli. Especially conspicuous are many cases of *phototropism*, either positive or negative, among protozoa, worms, insects, etc. Perhaps the most universal tropistic response is *galvanotropism; i.e.*, movement determined by the direction of an external electric current. Although such currents probably play no rôle in their natural lives, most animals move or orient themselves in the direction of a weak constant current passed through them—some animals toward the positive, others toward the negative, electrode. This response is shown even by man:

when a weak electric current is sent laterally through the head, the person leans toward the positive electrode, entirely involuntarily and without any conscious sensation whatever. Some animals—*e.g.*, many kinds of worms—exhibit positive *stereotropism*, which results in a tendency to crawl into corners or holes. Many animals exhibit *geotropism*, either positive or negative, tending to swim, crawl, or fly downward or upward as the case may be.

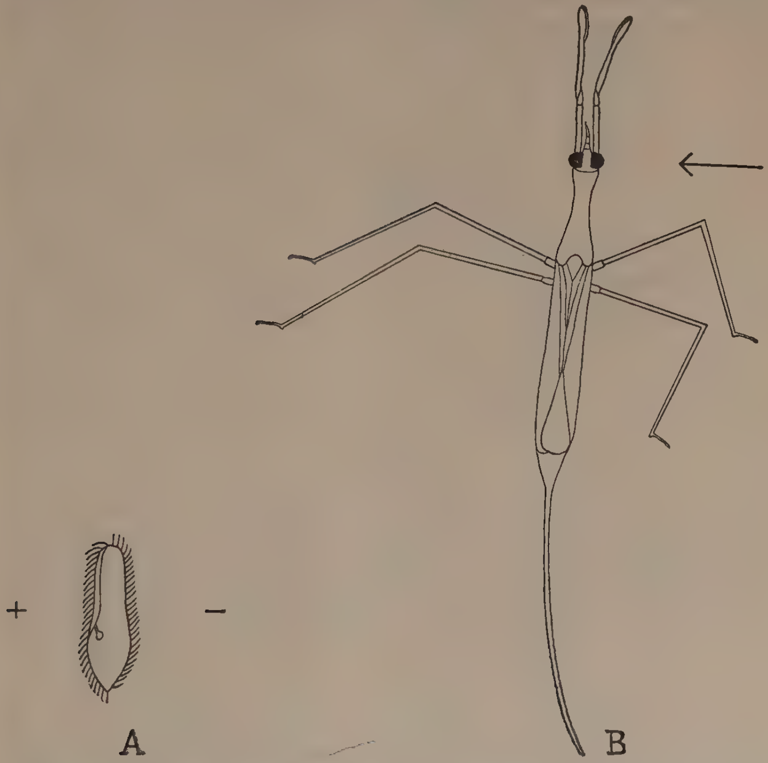


FIG. 108.—*A*, galvanotropic response of Paramecium to an electric current passing in the direction indicated by the signs; the reversal of the effective beat of the cilia on the side toward the negative electrode turns the animal automatically toward this electrode. *B*, phototropic response of Ranatra (an insect); arrow indicates direction of the incident light; the flexion of the legs on the illuminated side and extension of those on the other side turns the animal automatically toward the light. (*A*, after Loeb; *B*, after Holmes.)

The mechanisms of these responses are, obviously, very different in different kinds of animals; *e.g.*, the galvanotropic response in Paramecium is effected by cilia, in higher animals by muscles. The one factor common to all true tropisms is the unequal activity of symmetrically situated effectors on the two sides of the organism, due to the unequal stimulation of symmetrically situated receptors on the two sides: this automatically results in turning the organism until the symmetrically situated receptors of its two sides are equally stimulated; *i.e.*, either directly toward or directly away from the source of the stimulus (Fig. 108).

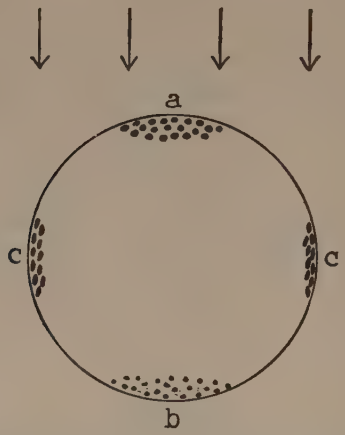


FIG. 109.—Diagram showing the difference between phototropism and response to intensity of light. The figure represents a circular glass vessel containing several kinds of animals; arrows indicate direction of the incident light. Positively phototropic animals collect at *a*; negatively phototropic animals at *b*; and animals which "avoid" the light, coming to rest in the shade, collect at *c*. where they are relatively shaded by the shape of the vessel. (After Loeb.)

Many activities of animals simulate tropisms, but are revealed by more careful study to be responses of a quite different kind. For instance, paramecia always congregate in a drop of weak acid, and this was at first ascribed to positive chemotropism toward the acid. Further observation, however, shows that no tropism, in the true sense of the word, is here involved: the paramecia swim into the acid by accident, but when they pass from weak acid into neutral water, the latter acts as a stimulus, producing the typical motor reflex (p. 334) of this organism, as a result of which they automatically swim back into the acid. This occurs whenever a paramecium swims from weak acid toward neutral water, but *not* when it swims from water to weak acid: as a result, all or most of the paramecia are sooner or later "trapped" in the drop of weak acid. Similar explanations have been found for many other cases originally thought to be due to chemotropism. Due to the failure to distinguish carefully between tropisms proper and these other types of response, there has been a great deal of unnecessary controversy on this subject. There can be no doubt, however, that true tropistic responses play an important rôle in the behavior of many lower animals as well as in plants. In the higher animals, they are less frequent and conspicuous, and become supplanted or modified by other, more complex, types of response.

Compound reflexes: instincts.—In the higher animals—*i.e.*, those with a central nervous system—while some stimuli may elicit only simple reflexes, involving the action of one small group of effectors, other stimuli initiate very complex series of responses, either simultaneous or successive. These compound reflexes are commonly called *instincts*. The line between simple reflexes and instincts is not at all sharp. In ourselves, sneezing, coughing, and swallowing are commonly classified as reflexes, while grasping, putting things into the mouth, sucking, biting, chewing, spitting out disagreeable objects, etc., are classed as instincts. The complexity of muscular movements involved in some of these "instinctive" actions is not much greater than in those called "simple reflexes." There is, in fact, so complete a gradation between the simplest reflexes and the most complex instincts that it is entirely arbitrary where the line is drawn between them.

On the other hand, it is often difficult to distinguish, in practice, between instincts and *habits*. These two types of complex responses are, however, theoretically distinct. Habits are responses determined, in part, by the *previous experience* of the individual; while instincts are, like tropisms and other simple reflexes, determined solely by the immediate stimulus and the inborn structure of the animal's responsive mechanisms. A purely instinctive action is therefore performed for the first time, without either practice or imitation, exactly the same as after a thousand repetitions. Indeed, some of the most complex instinctive responses are performed only once during the whole lifetime of the individual. In many insects, for instance, such acts as mating, egg-laying, cocoon-spinning, etc., occur but once in each lifetime; the animal, therefore, has obviously no opportunity to learn or improve these acts. Such instincts as these often bear no obvious relation to immediate external stimuli. While external conditions may hasten or delay, more or less, their initiation, the essential stimuli in many cases seem to be internal, *e.g.*, the completion of a certain stage of development in particular organs. Whether the initial stimulus be external or internal, the essential nature of these complex instinctive actions is a chain of reflexes, each response constituting a stimulus which arouses the next response, and so on.

A conspicuous feature of many instincts, as well as tropisms and other simple reflexes, is their "usefulness"; *i.e.*, they serve, in one way or another, to secure the welfare of the individual or the perpetuation of the race. This characteristic, however, does not imply any knowledge, on the part of the animal, of the consequences of its acts: it is, like the usefulness of a machine constructed to do a particular thing, a mechanical result of the nature and arrangement of its parts—receptors, nervous system, and effectors. The explanation of the usefulness of the behavior of an animal, as of a machine, lies in the causes that led to the production of a particular kind of structure; this question will be discussed in later chapters (Part V).

The "forced" nature of these responses is clearly shown by the fact that their usefulness applies only under the natural conditions of the animal's life; *i.e.*, those conditions under which the species has lived for many generations. When the animal is placed under artificial conditions, or when some feature of its natural environment is changed, it still responds in the same way to the same stimulus, even though the response may now be useless or injurious. Moths, for instance, are strongly positively phototropic. Under natural conditions, this response is probably a useful one, since the moths feed on flowers and many nocturnal flowers are white. With the introduction of fires, lamps, etc., into the moth's environment, this response becomes a suicidal one—but it persists nevertheless. The moth flies into the flame for the same reason that it flies to a white flower—not because it knows the flower is nutritious, or because it thinks the flame is a flower, but because its eyes, nervous system, and wing muscles are so connected that unequal illumination of the two eyes automatically turns it toward the light (p. 338). Artificial machines have been constructed which behave in exactly the same way. Such "automaticity" is characteristic of most of the behavior of invertebrates and the lower vertebrates. The most complex and apparently purposeful acts of insects, fishes, frogs, etc., are, in most cases, as machine-like as the bending of a plant toward the light—the machinery is merely more complex. Even in the higher vertebrates—birds and mammals—many of the activities most essential to their lives are purely instinctive, *i.e.*, independent of previous experience.

Modification of behavior.—While we have spoken of certain types of responses as being automatic and stereotyped, it is a familiar fact that all organisms exhibit, in varying degrees, plasticity of behavior; *i.e.*, the same stimulus does not invariably elicit the same response. Many factors may modify, to a greater or less extent, the usual response to a given stimulus.

Combinations of two or more stimuli, applied simultaneously or in fairly close succession, often alter the response which would be evoked by either one alone. This alteration may consist in (1) *reinforcement*, *i.e.*, a stronger response than usual; (2) *inhibition*, a weaker response or none at all (p. 304); or (3) *modification*, a somewhat or even entirely different response than either stimulus alone would evoke. All these phenomena depend on the particular connections, within the nervous system, of the several reflex arcs involved; and also on the time and intensity relations of the nerve-impulses in these various paths (p. 304). To some extent, similar factors may operate in organisms, such as plants and protozoa, without structurally distinct conduction paths. The behavior of an organism at any moment is, in general, determined not by a single stimulus but by the entire *situation*, *i.e.*, the aggregate of all the effective stimuli impinging on it at the moment.

Repetition of the same stimulus often results in some change of the original response, which may be increase, decrease, or modification of the response. The usual course of events is an increase in intensity of response during the first few repetitions of the stimulus, followed sooner or later by a decrease and eventually cessation or complete alteration of the response. The first phase—increase of response—is probably related to the phenomenon of summation of stimuli (p. 303); while the subsequent decrease is due to fatigue in some part of the conduction path, *e.g.*, the receptors, the central nervous system, myo-neural junctions, etc. (p. 305). In many cases, frequent repetition of the same stimulus may result in the substitution of an entirely different mode of response, simulating learning by experience; this result, however, may be due simply to fatigue in some part of the original conduction path; the new response may be due to summation of stimuli in some other path, or perhaps to the fatigue of neurones which previously inhibited it. These phenomena also appear, to some extent, in organisms without true nervous systems. In a sense, all these alterations of response by repetition of stimuli constitute modification of behavior by experience, since the response to any particular stimulus in the series depends, in part, on the effects of the previous ones; the phenomena mentioned here differ, however, from true *learning* in that the effects persist but a very short time—usually a matter of seconds or minutes only.

Finally, the response of an organism to any particular external stimulus or combination of stimuli always depends, more or less, on the *internal state* of the organism at the moment. This general term, "internal state," comprises a multitude of factors: stage of development, age, state of nutrition, activities of the reproductive organs, chemical conditions in the cells and body-fluids, etc. Not only the external situation, but also the organism itself, is changing from moment to moment. The total situation determining the behavior of a given organism at a given moment includes all factors, internal and external, capable of affecting its responsive mechanisms. The variability of the behavior of organisms is a necessary result of their being alive—that is, constantly changing. The unpredictability of their behavior is due simply to our ignorance of all the factors which may affect it.

Conditioned reflexes: habit and intelligence.—In the higher animals, especially the birds and mammals, a conspicuous feature of behavior is the persistent—permanent or semi-permanent—modification of response to a given situation by the *previous experience* of the individual; *i.e.*, by the effects of previous stimuli and the animal's own responses to them. This phenomenon is commonly called *learning*, *habit*, *memory*, etc. It is only within recent years that this type of behavior has been subjected to scientific methods of study and interpretation.

The classical experiments which initiated the scientific study of learning were performed on dogs. When a dog is given food, its salivary glands secrete. This is a simple reflex, independent of any previous experience. By a simple operation, the secretion of saliva may be observed from the exterior. With dogs so prepared, the presentation of food was accompanied by the ringing of a bell. After several repetitions of this combination of stimuli, it was found that the ringing of the bell alone, without the presence of food, would elicit the secretion of saliva. This sound, needless to say, did not evoke any such secretion in dogs not previously trained in this way. This type of response is called a *conditioned reflex:* its essential feature is the *substitution of one stimulus for another* by frequent *association of the two stimuli.* Similar experiments have since been performed on many other animals, including man, involving various types of responses—muscular as well as glandular—and of stimuli—visual, tactile, olfactory, auditory, etc. The experiments have been made more complex in various ways. A stimulus *B* may be substituted for the original stimulus *A*, *C* for *B*, *D* for *C*, and so on. The effect of one of the substituted stimuli, or even of the original one, may be inhibited by some other stimulus *X;* by frequent repetition of this inhibition *X* may be made a *negative stimulus* for this particular response; the effect of *X* may be inhibited by *Y*, which thus becomes a positive stimulus; etc. The method of conditioned reflexes has been used to determine the ability of animals to distinguish among different pitches of sound, different colors, etc. The more frequent the association of the original stimulus with the substituted stimulus, the longer does the conditioned reflex persist. In short, all those phenomena which we commonly call *learning*, *habit*, *memory*, etc., can be analyzed in terms of conditioned reflexes. On the ability of an animal to form conditioned reflexes depends its capacity to *profit by experience*, which we call *intelligence*.

The fundamental problem involved in a scientific explanation of intelligent, as distinguished from purely instinctive, behavior is therefore: how does one stimulus become substituted for another by frequent association with it? This question can not yet be answered with certainty. It is probably connected with the phenomenon of facilitation in the central nervous system, which, in turn, may be related to the supernormal phase of irritability in nerves and other types of cells (p. 297). We can only say with some assurance that a more or less permanent increase of penetrability has occurred at some point of the neural pathway, presumably at some synapse. We know in what part of the nervous system these effects occur; namely, the *cerebral cortex*. If a small portion of the cerebral cortex be removed, the animal may lose a definite group of conditioned reflexes, while retaining others unimpaired. If the whole of the cerebral cortex be removed, the animal loses not only all the conditioned reflexes already formed, but also its entire capacity to form any new ones. Most of its original reflexes, even fairly complex ones—instincts—may remain quite unimpaired. If we compare various kinds of vertebrates—fishes, amphibians, reptiles, birds, mammals—we find, also, that their intelligence, or ability to form conditioned reflexes, is closely correlated with the relative development of the cerebral cortex. This faculty, however, is not entirely lacking in some of the higher invertebrates: what part of the nervous system of these animals may serve this function is still unknown.

It is very difficult to say just where, in the animal kingdom, intelligence—the ability to form conditioned reflexes—first appears. Deceptive appearances of habit formation occur in all organisms. Besides the very transitory summation and fatigue effects previously mentioned, more permanent modifications of response may be caused by injury, mechanical changes in skeletal or muscular structures, etc. Such effects are obviously different in nature from conditioned reflexes, but not always easy to distinguish from them in practice. The ability to learn by experience has thus been attributed, by various observers, to such animals as worms, starfish, coelenterates, and even protozoa. The evidence, however, when more critically examined, does not seem to prove any more ability to learn in these animals than in plants.

In some of the higher invertebrates—arthropods and molluscs—there is more conclusive evidence of a certain, though very limited, educability. Conditioned reflexes have been demonstrated, apparently quite conclusively, in crabs, snails, and octopi. Such responses form, however, an extremely small part of the behavoir of these animals, and probably play no important rôle in their natural lives. What little intelligence they may possess they could probably get along just as well without.

In some of the insects this type of behavior seems to be more frequent and significant. The maximum development of intelligence in this group is found in the social insects—ants, bees, and wasps. The ability of bees, for instance, to find their way home has been clearly shown, by many experiments, to depend upon the individual experience of each bee. It should not be supposed for a moment, however, that the complex social organizations and cooperative activities of these insects are manifestations of intelligence—for the most part their behavior consists of inborn, essentially unmodifiable, instinctive responses to particular situations.

The cold-blooded vertebrates show, on the whole, scarcely more intelligence than some of the insects mentioned above. Fishes, amphibians, and reptiles are all capable of forming conditioned reflexes and can be "trained" to a certain extent; but learned responses play, at most, an extremely minor part in their behavior.

Birds and mammals stand strikingly above all other animals in their ability to learn, and also in the part played by learned responses in their natural behavior. There is a very distinct gradation in intelligence within each of these classes. Among the mammals, in particular, there is a marked correlation between the intelligence of the various species and the relative development of their brains, especially of the cerebral cortex. A high degree of educability, as compared with most other animals, is attained by some of the larger carnivores and herbivores, such as dogs, horses, and elephants. These animals are not intelligent *because* they are domesticated—they are domesticated because of their intelligence, *i.e.*, their ability to be trained. The highest development of intelligence, however, is found in the group of Primates—monkeys, apes, and man. There can be no doubt that monkeys—even after making all due allowance for their enormous advantage in the possession of hands—display distinctly more intelligence than the four-footed mammals. Monkeys quickly learn to employ tools as means to an end—*e.g.*, a stick to secure food which is out of reach; they display more initiative and curiosity than other animals; in these features their behavior approaches that of man. There is also evidence that the anthropoid apes—which resemble man most closely in the structure of their bodies and especially of their brains—are more "human" in their behavior than the tailed monkeys.

Behavior of man: language.—The older point of view on human behavior was to regard it as sharply distinct from that of other animals: man was said to act by "reason," all other animals by "instinct." We have already seen that no such sharp distinction can be drawn; man displays many simple reflex and instinctive responses, while many of the higher animals show more or less intelligent behavior. On the other hand, many writers, in attempts to minimize the differences between human and other animal behavior, have perpetrated highly exaggerated accounts and utterly uncritical interpretations of the "intelligent" behavior of animals. The truth probably lies in the other direction: far more of human behavior than is commonly supposed is purely instinctive, emotional, or imitative. For all this, there is no denying the enormous gap between the achievements of man—at least of civilized man—and those of any other animal. The essential clew to this difference seems to lie in one peculiar feature of human behavior: *language.* Every known race of man has some kind of language, and there is no good evidence that any other animal has.

A *word* is both a response and a stimulus: on the one hand, it is a conditioned reflex which may be elicited by a variety of substituted stimuli; on the other hand, it is a stimulus which has been substituted for many other stimuli. In short, a word is a relatively simple motor act which "sums up" a vast amount of experience. This is the distinction between words and purely instinctive or emotional sounds, which are uttered by many animals: a word is a vehicle of experiences. *Language* consists not merely of words, but of *combinations of words*. The separate words are, in general, purely imitative, but the combinations are largely original. Every conditioned reflex involves an element of originality, in a sense; that is, it represents a new combination of stimuli and responses, so far as the individual animal is concerned. Language may be described as a mode of behavior which enormously extends the range, and decreases the time and labor of acquisition, of original individual responses.

Language may be said to have two general functions in human behavior: an individual and a social function. It enables the individual to handle a vast amount of past experience economically and expeditiously. There is a difference of opinion, among students of the subject, as to whether *thinking* necessarily involves the muscles of speech or only the nervous system; but, however this may be, there can be no doubt that all our thinking of any abstractness or generality is done in words—and it is precisely this kind of thinking which constitutes that feature of human behavior which we call *reason*. In addition to this reasoning function in the individual, language—spoken or written—is the instrument of *intelligent* and *progressive*, as distinguished from instinctive or merely imitative, *social cooperation*.

It is probably no exaggeration to say that all the distinctive features of human behavior—as compared with that of other higher animals—rest on this one primary difference, language. The powers of understanding and using language depend on certain particular regions of the cerebral cortex, whose injury or disease results in loss of these powers. The regions thus identifiable as *language centers* are much more highly developed in man than in any other animal; indeed, the greater development of these regions constitutes the most conspicuous visible difference between the brains of men and those of apes.

It will be noticed that, in speaking of human and other animal behavior, we have not found it necessary to introduce such words as "consciousness," "purpose," and "will." These words, as popularly used, correspond roughly to certain rather vaguely defined aspects of the behavior of higher animals, especially man; but the apparent impossibility of agreeing on generally acceptable objective definitions renders them useless for scientific purposes. Where the attempt has been made to use these words in any precise sense, they seem to have contributed toward obscuration rather than elucidation of the facts. We have seen that no very sharp lines can be drawn at any point between the behavior of the very simplest organisms and that of the most complex, including man. The differences in complexity of behavior seem to depend chiefly on the number and form of the conduction paths from receptors to effectors; the processes involved, in receptors, conductors, and effectors, are chemical and physical changes which differ only in degree of complexity from those occurring in non-living systems. The activities of a steam engine, an amoeba, or a man depend, in the final analysis, on essentially the same factors: the fundamental properties of matter and energy. Each is a machine whose behavior at any moment is determined by the totality of all factors, external and internal, affecting it at that moment, together with the past history of the machine which has made it what it is at the moment. The more complex, chemically and structurally, is the machine, the more different kinds of factors can affect it, and, consequently, the more variable and unpredictable will be its behavior.

CHAPTER XVIII

GROWTH AND CELL DIVISION

One of the most characteristic properties of living matter is *growth*. The term growth, as applied to organisms, implies more than mere increase in size: a cell immersed in a hypotonic solution increases in size, by taking up water, but we do not regard this as growth. The phenomenon of growth, as exhibited in living systems, involves at least three kinds of processes: (1) *chemical synthesis* of the components of protoplasm and of accessory materials (skeletal materials, etc.); (2) *morphogenesis*, the elaboration of these substances into the characteristic structures of cells and organisms; and (3) *multiplication* (increase in number) of the organized units of living matter—intracellular structures, cells, and organisms. In practice, these three kinds of processes are always inextricably intermingled. When we are thinking primarily of increase in the *amount* of protoplasm and other materials making up the organism, we speak of *growth;* when we have chiefly in mind the progressive production of specific form, we call the process *development;* when our attention is directed to the increase in *number* of discrete units—cells or individual organisms—we speak of *reproduction*. Actually, however, each of these phenomena involves all three of the kinds of processes mentioned above: chemical synthesis, morphogenesis, and multiplication.

The growth of a multicellular organism involves increase in size of the individual cells (and of the intercellular structures), increase in the number of cells, and differentiation, both chemical and structural, among the cells as well as within each cell. Reproduction and development of multicellular organisms involve these same processes. The phenomena of growth, development, and reproduction, in multicellular as well as unicellular organisms, are fundamentally *cell* activities.

Assimilation and growth.—We have already learned that one phase of metabolism in every cell—though varying greatly in relative amount in different cells—is *constructive metabolism, i.e.*, the synthesis of more complex chemical compounds from food substances or their fragments. Among the substances thus synthesized are stored food substances (starch, fats, etc.), skeletal materials (cellulose, etc.), secretion products (enzymes, hormones, etc.), and the essential components of protoplasm itself: proteins, lipins, etc. These chemical syntheses are effected by the catalytic activity of intracellular enzymes. But these catalysts have themselves been produced in the cell by its own previous constructive metabolism. The synthesis of protoplasm is therefore an "endless chain": the chemical activities of living protoplasm result in the production of more protoplasm, and so on. This phase of metabolism—the production by the living protoplasm of *more material like itself* out of foreign materials (*i.e.*, food substances)—constitutes *assimilation.*

Assimilation results in increase of the amount of protoplasm and therefore of the size of the cell. *Growth* of the cell is therefore a direct result of assimilation. But cells do not increase in size indefinitely; most kinds of cells, in fact, never exceed microscopic dimensions. When a cell reaches a certain size—which varies according to the kind of cell and the surrounding conditions—it either ceases to grow or it *divides into two cells.* These, in turn, may grow up to their maximum size and divide again; and so on. The growth or a multicellular organism consists chiefly in this increase in *number of cells*, rather than in the size of the individual cells. In differentiated multicellular organisms, many of the cells —particularly the more specialized types of cells—cease to grow and divide after a time; but certain kinds of cells may go on growing and dividing indefinitely. Some of these "potentially immortal" cells may, under proper conditions, separate from the multicellular body and develop—by further growth, divisions, and differentiation—into new multicellular individuals like those from which they came: this constitutes *reproduction.* In unicellular organisms every cell division, of course, constitutes reproduction, since each of these cells is a separate individual. All processes of growth and reproduction, in multicellular as well as in unicellular organisms, are therefore essentially processes of cell growth and cell division.

Mitosis.—The normal process of cell division, called *mitosis*, is one of the most complex and at the same time one of the most regular processes in living things. The microscopically visible aspects of mitosis are most conveniently studied in cells which have been *fixed* (*i.e.*, killed instantaneously and coagulated by chemicals which prevent decomposition and disintegration), *stained* with dyes which stain the various intracellular structures differentially, and *sectioned* into very thin slices which can be studied microscopically by transmitted light. This method has the obvious disadvantages that we cannot follow the sequence of events in a single cell and that we cannot be sure how accurately the fixed and stained section represents the normal structures of the living cell. In exceptionally favorable material, however, all the essential features of mitosis can be observed in the living cell; and such observations confirm the general conclusions drawn from the study of fixed sections. Each cell that we see in fixed sections must be regarded as a "snapshot" taken at a particular moment of a continuous process; by arranging these "snapshots" in the correct sequence, we can construct a "moving picture" of the whole process. The details of mitosis differ somewhat in different kinds of cells, although its essential features are the same in all. We may examine first the process in typical higher plant cells, such as the cells of the rapidly growing root tip of an onion (Fig. 110).

During the growth, or so-called "resting," stage—*i.e.*, the non-dividing stage—of the cell, the nucleus is delimited from the cytoplasm by a definite *nuclear membrane;* the *chromatin* is invisible in the living nucleus, but in stained sections it appears as a fine, irregular network staining with certain dyes called "nuclear stains" (Fig. 110, *1*). The first visible sign of mitosis is the aggregation of the chromatin into a number of long slender threads, the *chromosomes*. In the onion there are always 16 chromosomes in each cell; in other organisms the number is different, but is generally the same in all the cells of any one species (p. 355). These threads gradually contract, growing shorter and thicker.

At some time during this process, or even earlier, *each chromosome splits lengthwise into two exactly similar halves.* During this stage also, the nuclear membrane disappears completely, leaving the chromosomes free in the cell. In the nuclear region appears a spindle-shaped group of fibers, which converge toward opposite ends of the cell. Some of these fibers are attached to the chromosomes—one to each of the halves of each chromosome—while others run directly from one pole of the spindle to the other. All these stages are called the *prophases* of mitosis (Fig. 110, *2–7*).

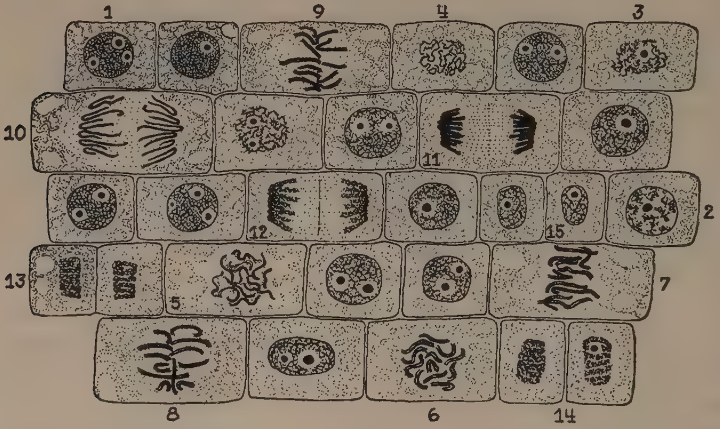


FIG. 110.—Portion of section of root tip of onion, fixed and stained, showing cells in various stages of mitosis. *1*, intermitotic or "resting" stage; *2–7*, prophases; *8*, *9*, metaphases; *10*, *11*, anaphases; *12–14*, telophases; *15*, intermitotic stage just after completion of mitosis.

The chromosomes now take up a position in the equatorial plane of the spindle, *i.e.*, in the middle of the length of the cell. This stage is called the *metaphase* (Fig. 110, *8*, *9*).

The two halves of each chromosome, formed by the longitudinal split, now move toward the opposite poles of the spindle, *one half of each chromosome going to each pole.* The movement of the chromosomes looks as though each half-chromosome is being pulled toward its respective pole by the spindle fiber attached to it. These stages are called the *anaphases* (Fig. 110, *10*, *11*).

When the *daughter chromosomes*—as the threads resulting from the longitudinal split are called—arrive at their respective poles, they become crowded closely together. Then they become vacuolated, spin out, and reconstitute a diffuse network; during this time a new nuclear membrane is formed about them—and two *daughter nuclei* have been formed. Those spindle fibers which are not attached to the chromosomes contract toward the equator of the spindle, and finally form a partition, called the *cell plate*, across the middle of the cell. This partition then splits into two parallel plates between which a new *cell wall* is formed, dividing the cell into two *daughter cells*. These stages, during which the daughter nuclei are formed from the two groups of daughter chromosomes and the cytoplasm is divided into two daughter cells, are called the *telophases* (Fig. 110, *12–14*).

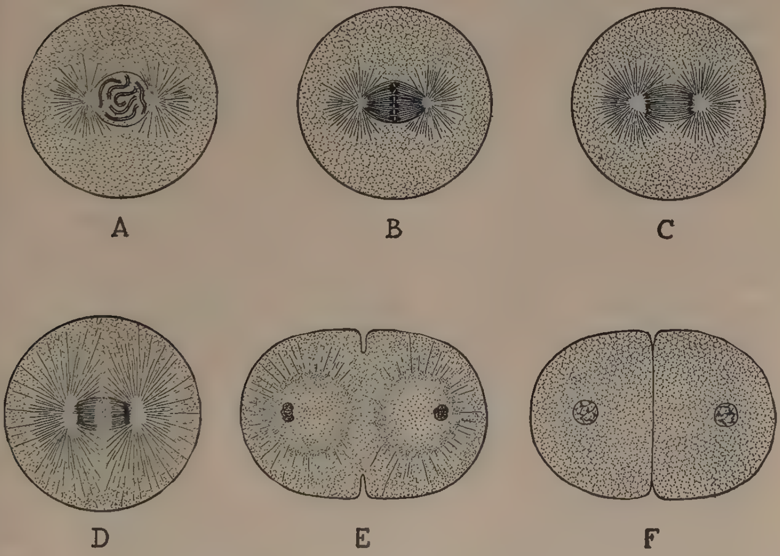


FIG. 111.—Echinoderm egg-cells, fixed and stained, in various stages of mitotic division. *A*, prophase; *B*, metaphase; *C*, anaphase; *D*, early telophase; *E*, later telophase, with cleavage of the cytoplasm beginning; *F*, intermitotic stage just after completion of division. (Adapted from Fry.)

In many cells of higher animals, the visible aspects of mitosis are further complicated by the appearance of two large radiate structures, called *asters*, in the cytoplasm, one at each end of the dividing cell (Fig. 111). These may enlarge until they occupy the entire cell outside of the spindle. At the center of each aster is a smaller spherical region, called the *centrosome*, toward which the spindle fibers converge. The cytoplasm of the animal cell is also divided in a different way than in the plant cell. No cell plate is formed, but during the telophases a furrow appears about the equator of the cell, which gradually deepens until it cuts the cytoplasm in two, forming two daughter cells (Fig. 111).

There are variations in many details of the mitotic process in different kinds of cells, especially in regard to the behavior of the non-chromatinic portions of the cell; but the division and distribution of the chromosomes are essentially the same in all multicellular organisms at least. Mitosis in the simpler organisms will be discussed later (p. 358).

The duration of the mitotic process varies, in different kinds of cells, from a few minutes to several hours, the prophases and telophases being usually the longest. The duration of the intermitotic ("resting") stage is even more variable: in rapidly developing tissues, one mitosis may succeed another with practically no interval at all; in the differentiated tissues of multicellular organisms, on the other hand, mature cells may remain in the "resting" stage, without further division, throughout the remaining lifetime of the organism, *i.e.*, for many years.

The significance of mitosis.—Mitosis may be said to accomplish three things: (1) the division of one cell into two; (2) the mixing of the nucleoplasm and cytoplasm; and (3) the *exactly equal* distribution of the chromatin to the two daughter cells.

(1) The division of one cell—specifically of the cytoplasm—into two at each mitosis results in the subdivision of protoplasm into units of definitely delimited, usually microscopic, size. The primary significance of this cellular type of organization seems to lie in the relation of *surface* to *volume* of protoplasm. The surface of a sphere, a cube, or any symmetrical solid is proportional to the *square* of its diameter, while the volume is proportional to the *cube* of the diameter. As a cell increases in size, its volume therefore increases at a greater rate than its surface; *i.e.*, the *ratio* of surface to volume decreases. A cell absorbs all its food substances, and excretes its waste products, through

its surface. Should an undivided solid mass of protoplasm increase in size indefinitely, it would soon reach a point where the interior would be starved, asphyxiated, or poisoned by its own waste products. The division of the cell into two cells, however, increases the surface of the protoplasm without increasing its volume, thus maintaining a surface-volume ratio compatible with the necessities of absorption and excretion. The only organisms which consist of undivided masses of protoplasm (syncytia) have shapes which present a relatively large exterior surface; *e.g.*, very flat and irregularly lobose, or very slender and branching (Figs. 13, 35). Plant cells are, on the average, larger than animal cells; this is correlated with the presence in the former of a large central vacuole, so that the protoplasm is spread out in a thin layer having a large surface-volume ratio.

Another significant aspect of the cellular subdivision of protoplasm is the *differentiation* among cells which we have seen to characterize all the higher organisms. Neither unicellular nor syncytial organisms ever remotely approach, in either size or complexity, the multicellular ones—those whose protoplasm is subdivided into discrete cell units.

(2) The dissolution of the nuclear membrane during mitosis results in the mixing of the nucleoplasm and the cytoplasm. This may have something to do with the increased capacity for growth shown by the cells after mitosis, perhaps by liberating into the cytoplasm substances, such as enzymes, produced in the nucleus, to which the nuclear membrane is ordinarily impermeable. In some cases it is definitely known that certain properties of the cell change markedly immediately after the dissolution of the nuclear membrane.

(3) The most striking feature of mitosis is the exactly equal division and distribution of the chromatin material. This is not merely a quantitatively equal partition of the total mass of chromatin, but an exact division of each individual chromosome and the distribution of one half of each chromosome to each daughter nucleus. This results in maintaining a constant number of chromosomes in all the cells of an individual organism. This number is also, in general, constant for the cells of all individuals of the same

species, and is usually an even number; the significance of these facts will appear more fully later (Chapters XIX-XXII). The chromosome number varies, in different organisms, from 2 to 200 or more, but is usually between 12 and 36. Not only the number of chromosomes, but also the size and shape of each chromosome, are extremely constant; there are often considerable differences, in these respects, among the individual chromosomes of a cell, but exactly the same set of chromosomes appears in every mitosis of the individual and of the species. The chromosomes which appear in any cell during the prophase are exactly the same as those which apparently disappeared during the preceding telophase. In some cases, the separateness of the chromosomes can be seen at all times throughout the intermitotic ("resting") stage; in most cases this can not be seen directly, but there is conclusive evidence of other kinds (Chapter XXII) that it is always true. In other words, *each chromosome has a persistent individuality* —growing during each intermitotic period and dividing at each mitosis, but maintaining its own peculiar composition and structure throughout innumerable cell-generations.

The precision of the division of the chromatin material goes even further than the individual chromosomes, however. The chromosomes never divide transversely or diagonally, but always *longitudinally; i.e.*, each thread splits lengthwise throughout its whole length. The significance of this peculiar mode of division is that each chromosome consists, not of a homogeneous mass of material, but of a large number of qualitatively different particles—the *genes* —arranged in a linear series, *i.e.*, like beads on a string. The longitudinal splitting of the chromosome therefore effects the *division of each individual gene into two;* and the precise distribution of the daughter chromosomes insures that *every cell of the organism has exactly the same set of genes.* This seems to be the fundamental significance of the elaborate machinery of mitosis.

In contrast to the very precise division and distribution of the chromatin, the division of the cytoplasm appears to be, in general, a simple mass division. While this division is a fairly equal one in most cases, there are many cases where it is extremely unequal. The formed bodies of the cytoplasm also, in most cases, show no very exact equality of distribution to the two daughter cells. Plastids, and perhaps some other types of formed bodies (p. 25), grow and divide within the cytoplasm, but their divisions do not, in general, have any special relation to that of the cell as a whole. There appears to be no special machinery for the distribution of these bodies to the two daughter cells. This distribution is, on the whole, *approximately* equal (when the division of the cytoplasm is approximately equal) but is *not exactly* equal, either quantitatively or qualitatively. Any of these cytoplasmic formed bodies—plastids, etc.—may, in some cases at least, be formed *de novo* from the general cytoplasm; *i.e.*, they do not necessarily always originate by division of pre-existing bodies of the same kind. The same is true of *nucleoli* (p. 22), which always disintegrate during mitosis, and are formed anew in the "resting" nucleus (Fig. 110). In this respect the chromosomes stand in striking contrast to all other intracellular structures, for *chromosomes never originate in any other way than by division of pre-existing chromosomes;* and this division, as we have seen, is related in a very precise way to the mitotic division of the cell as a whole.

The mechanism of mitosis is one of the most difficult problems in biology. The formation, division, and regular movements of the complex mitotic structures in a liquid or gel system such as protoplasm indicates a complex of physical forces of whose nature and origin we have, as yet, scarcely an inkling. There are a number of theoretically, and sometimes experimentally, separable phenomena involved; *e.g.*, the condensation and splitting of the chromosomes, the dissolution of the nuclear membrane, the formation of the spindle, asters, etc., the movements of the chromosomes to the equator of the spindle and thence to the poles, the division of the cytoplasm, etc. Many hypotheses have been proposed and many non-living models constructed, in attempts to explain some one or more of these phenomena, but none of these can be said to have afforded, as yet, a satisfactory solution of the problems.

In recent years studies of the living cells by various methods have given us some information on the real nature of the mitotic structures whose "pictures" we see in the stained sections. The chromosomes are found to be jelly-like bodies which can be pulled around within the cell, and even pulled out of the cell, by very fine needles; when removed from the cell they quickly disintegrate. The asters, formed in many animal cells during mitosis, are found to be fairly solid bodies which increase in size by gelation of the protoplasm outward from their centers. The radiating astral rays (Fig. 111) are hollow channels through this solid structure, through which liquid protoplasm flows from its periphery into the centrosome, which is also liquid. The expansion of the asters during mitosis may help to effect the elongation of the cell and perhaps also the division of the cytoplasm—but these processes occur also in cells which have no asters. The spindle can also be pulled out of the cell as a fairly solid body. It is difficult to determine whether the chromosomes are really "pulled" or "pushed" toward the opposite poles during the anaphase, but there can be no doubt that the force which moves them, whatever its nature may be, is exerted—as shown by the shapes of the chromosomes in living as well as fixed cells—at precisely the points where the spindle-fibers appear (in stained sections) to be attached. The point of attachment of the spindle-fiber to the chromosome is, moreover, remarkably constant for each individual chromosome. The original splitting of the chromosomes, however, is quite independent of any of the other mitotic phenomena, since it usually occurs first and may, in exceptional cases, not be accompanied or followed by cell or even nuclear division. It is very hard to determine just when this split, which is the most essential feature of mitosis, actually occurs, as the split is difficult to see until the threads have shortened and thickened somewhat. It is very probable that the chromosomes—or at least the individual genes—actually divide during the "resting" stage, before the beginning of mitosis, or perhaps even earlier. The separation of the daughter chromosomes during mitosis must involve some very specific "repulsion" between them, since the two daughter halves of each chromosome *always* go to opposite poles.

Mitosis in the simpler organisms.—It might be expected that in the simplest organisms—bacteria, protozoa, etc.—we should find simpler types of cell division which might throw some light on the complex mitotic process in higher plants and animals. In fact, we do find among these organisms many intergradations between what appears to be a simple *amitotic* division of the cell (p. 360) and typical mitosis just like that of higher organisms. More careful study, however, of the supposed cases of amitotic division among these simple organisms tends to show that these also represent, in reality, simple forms of mitosis, involving some mechanism for more or less precise division and distribution of the chromatin.

In the bacteria, it will be recalled, there is no distinct nucleus; or, as it would be more logical to say, there is no distinct cytoplasm, since the chromatin is distributed more or less throughout the cell. Most of the bacteria are too small to permit clear observation of the mode of distribution of their chromatin at cell division; but in those forms which are large enough, there appears to be quite generally a tendency for the chromatin to be aggregated at the equator of the cell and distributed equally to the two daughter cells. Whether this involves the division and precise distribution of the individual chromatin granules is very difficult to determine, but in some cases at least this is stated to occur. In the Cyanophyceae, which resemble the bacteria in having no distinct nuclear membrane, there occur many intergradations between this very simple type of mitosis and forms with definitely organized chromosomes which split longitudinally at cell division (Fig. 112). In many of the protozoa the mitotic figure is entirely intranuclear and the nuclear membrane does not disintegrate at

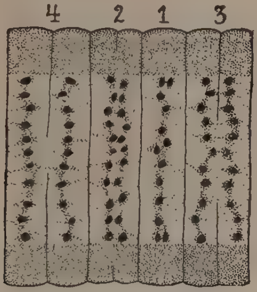


FIG. 112.—Cells of Oscillatoria, a colonial blue-green alga, showing a simple type of mitotic division. *1*, *2*, *3*, *4*, successive stages of cell division. (Adapted from Olive.)

any time during mitosis (Fig. 114). There is every gradation in the organization of the chromatin in this type of mitosis, from species in which it is in the form of numerous separate granules (as in the bacteria) to those with a definite small number of thread-like chromosomes which split lengthwise. Finally, some of the protozoa exhibit mitosis exactly like that in higher animal cells, including the asters. Most of the thallophytes (algae and fungi) also exhibit this type of mitosis, resembling in this respect the higher animals rather than the higher plants, in almost all of which asters are entirely absent.

In general, the phenomena of mitosis in these lower organisms are as yet much less completely known than in the higher plants and animals.

Amitotic division.—In many specialized types of cells, in higher organisms, the nucleus may divide by a simple process of constriction, without the appearance of chromosomes or any kind of mitotic figure. This type of nuclear division is called *amitosis*. In the great majority of cases, it is not followed by cell division. These separate fragments of the nucleus always, so far as known, fuse together again before or during the next mitotic division; their separation is therefore only temporary, and has no different significance than the branching form assumed by the nuclei of many metabolically active cells (Fig. 9). These nuclear fragments undoubtedly represent whole chromosomes or groups of chromosomes in the diffuse (*i.e.*, intermitotic) state.

In some kinds of cells, amitotic division of the nucleus may be followed by division of the cytoplasm (Fig. 113). Such division always represents a degenerative condition so far as the cells involved are concerned, though it may be perfectly normal for the organism; *i.e.*, such cells are nearing the end of their usefulness. "When once a cell has undergone amitotic division it has received its death-warrant; it may indeed continue for a time to divide amitotically, but inevitably perishes in the end." In particular, no cell which has originated by a true amitotic division has ever been shown to exhibit subsequently a normal mitosis; and such cells never take part in reproduction of the organism.

Many cases of supposed amitotic division have been subsequently shown to be merely abnormal appearing—though essentially regular—mitoses, due to certain abnormal conditions. As explained in the preceding section (p. 359), many cases of supposed amitotic division in even the simplest organisms now appear rather to represent very simple types of mitosis; but the whole organization of the nucleus is probably so much simpler in some of these forms that this distinction may be of less significance in them. It may be noted that in the ciliates (Paramecium, etc.), the *macronucleus* (Fig. 27) divides amitotically, while the *micronucleus* divides by a type of mitosis; the former, however, is shown by other evidence not to be a true nucleus, and always disintegrates at a certain stage of the life cycle of these organisms (p. 370).

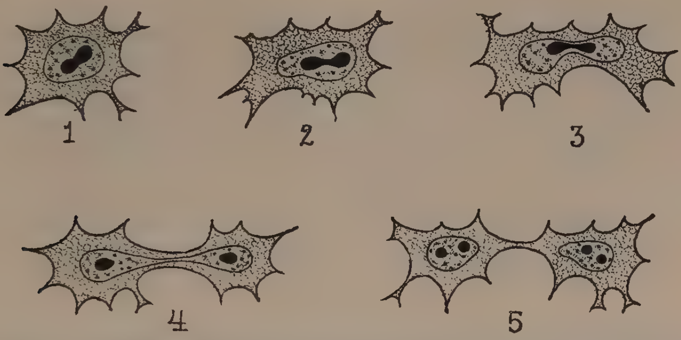


FIG. 113.—Amitotic division of connective-tissue cells. Stages *1–5* (selected from fixed and stained preparations) are presumed to represent successive stages of amitotic cell division. (After Novikoff.)

All these facts emphasize further the importance of the regular division and distribution of the individual chromatin particles, which is the distinctive feature of normal—*i.e.*, mitotic—cell division. As we shall see in the following chapters, this process is an essential factor in all the phenomena of reproduction and heredity.

CHAPTER XIX

REPRODUCTION OF SIMPLE ORGANISMS

It is a familiar fact that every kind of organism produces new individuals of its own kind. The mechanisms by which this is effected are of various types, among different kinds of organisms; all such processes are included in the general term *reproduction*. Every process of reproduction consists, essentially, in the separation from the parent organism of part of its protoplasm, which forms the new individual. At the basis of all modes of reproduction, therefore, as previously emphasized, are the processes of cell growth and cell division.

In unicellular organisms, ordinary cell division is obviously a mode of reproduction, since it results in the production of two individuals—*i.e.*, two separate and independent cells—from one; in this case we can not speak of "parent" and "offspring," since each new individual is half of the original one. In some unicellular organisms there are also special types of reproduction by cell division differing from this simple form (pp. 364–366). In colonial and multicellular organisms, the portion separated to form the new individual may consist of a single cell or of a group of cells. In the former case, the processes involved are similar to those of unicellular organisms; in the latter case, the separated portion may consist of a large part, up to half, of the original organism.

All the modes of reproduction hitherto mentioned, *involving only cell division and the separation of its products*, are called *asexual reproduction*. On the other hand, all organisms, except the very simplest (bacteria, some protozoa, etc.), exhibit also the opposite phenomenon: *the fusion of two cells* (or of their nuclei) *to form one;* this is called *sexual reproduction.*

In unicellular organisms sexual reproduction is always less frequent than asexual reproduction (cell division); in most multicellular animals, on the other hand, it is the most important and often the only mode of production of new *individuals*.

These various modes of reproduction will be discussed in more detail in this and the following chapters.

Binary fission.—The simplest and most common type of asexual reproduction of unicellular organisms is simple cell division, in which the cytoplasm as well as the nucleus is divided into two equal parts: this is called *binary fission*. In the very simplest forms, this appears to be a simple mass division; but, as previously indicated (p. 359), in most or all forms large enough to reveal the nuclear phenomena, more careful study tends to reveal a more or less simplified type of mitosis. In many species specialized cytoplasmic structures, such as flagella, chloroplasts, vacuoles, etc., are also divided equally in the process of fission. In very simple forms (bacteria, amoebae, etc.), the two cells formed by binary fission are practically identical with the parent cell except in size; they have merely to grow by assimila-

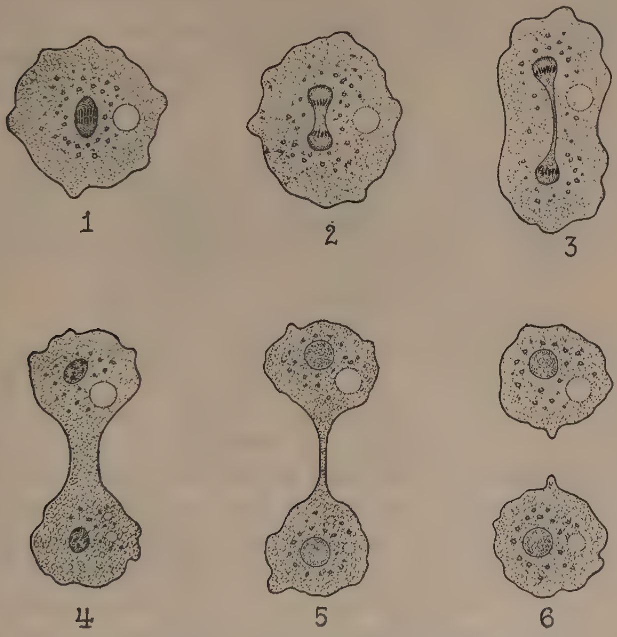


FIG. 114.—Binary fission of Amoeba (nuclei stained).

tion, divide again, and so on. In more highly differentiated forms (such as ciliates, etc.), the daughter cells, after fission, undergo also a process of morphogenetic development to reconstruct the complex intracellular structures.

In motile forms (most protozoa, free-swimming algae, etc.), the two cells formed by binary fission usually separate completely, swimming or crawling away from each other; such species therefore remain strictly unicellular. But in non-motile forms (many bacteria, Pleurococcus, etc.) the cells often adhere to each other temporarily, forming *colonies* of loose and indefinite form. Such colonies are readily broken up by any kind of mechanical disturbance, such as water currents. Some of the simplest types of definitely colonial algae, such as Spirogyra, differ from the foregoing only in that the planes of cell division are all parallel to each other, forming a linear aggregate of cells which adhere to each other by flat transverse cell walls. These filaments may also be broken up by mechanical disturbances, or by the death of some of the intermediate cells. In such colonies, there is evidently no real distinction between reproduction of the individual cells (cell division) and that of the whole organism, *i.e.*, the colony. Most colonial and multicellular algae, however, have more specialized modes of reproduction (p. 366).

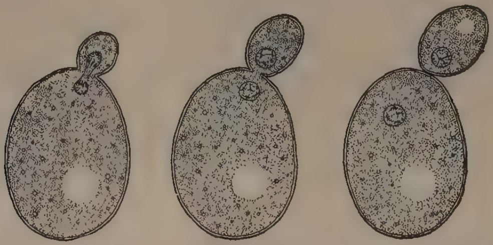


FIG. 115.—Budding of yeast cells (stained to show the nuclei).

Budding is a form of cell division in which the *cytoplasm* is divided very unequally, although the division of the nucleus is equal as usual. The most familiar examples of this are the yeasts (Fig. 115). These cells usually remain attached temporarily. The smaller cell ("bud") may divide again, in the same way, before it has grown to the size of the parent cell, thus producing a still smaller bud. This process results in a cluster of cells of various sizes, sometimes attaining the appearance of a small branching filament; these cells, however, do not form a definite or permanent colony.

There are also many examples of budding among the protozoa.

Spore formation is a mode of asexual reproduction of widespread occurrence among both simple organisms and higher plants. This consists of a series of nuclear and cytoplasmic divisions within the original cell wall or membrane of the parent cell, resulting in a number of small cells, called *spores*, which are eventually liberated by the disintegration or rupture of the original cell wall or membrane.

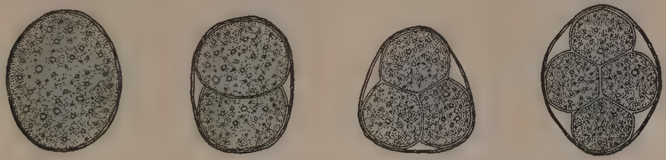


FIG. 116.—Spore formation in yeast cells (unstained).

The yeasts exhibit a simple type of spore formation. At certain times (especially under unfavorable conditions, such as dryness) the nucleus and cytoplasm divide into four equal parts, forming four spores, each with its own cell wall, but all contained within the original cell wall (Fig. 116). Eventually the spores are liberated from the old cell wall and, under favorable conditions, resume growth and multiplication by budding. Most of the more complex fungi also reproduce by means of spores similar to those of yeast; the number of spores formed by a single cell varies in the different groups.

Some species of protozoa reproduce asexually by sporulation. The spores may be, in different species, amoeboid, flagellate, or non-motile; they are often produced in very large numbers. This process often alternates with binary fission, or with sexual modes of reproduction. Sporulation is of especially frequent occurrence among parasitic protozoa.

Many species of algae reproduce asexually by means of free-swimming flagellate spores, called *swarm-spores* or *zoospores.* In some cases the whole protoplasm of an ordinary non-motile cell forms a single zoospore, which escapes by rupture of the cell wall; more frequently, several or many zoospores are formed from a single cell, as in the cases described above. The zoospores, after swimming about for a time, develop by growth and cell divisions into the ordinary form of the plant again (Fig. 117).

Some of these types of reproduction by means of spores serve other functions besides mere multiplication, *i.e.*, increase in number of individuals. In non-motile algae, the swimming zoospores effect a wider *dispersal* of the species. The non-motile spores of yeasts and other fungi are more resistant to unfavorable conditions, especially drying, than the ordinary cells: they serve for *protection* during unfavorable conditions, and permit dispersal through the air. Very resistant cells, called *resting spores*, are formed by many bacteria and Cyanophyceae; these are not really mechanisms of reproduction at all, since only one of these spores is formed from a single ordinary cell, but simply mechanisms of protection against unfavorable conditions—drying, heat, cold, etc. Similar structures are formed by many protozoa, where they are usually called *cysts*.

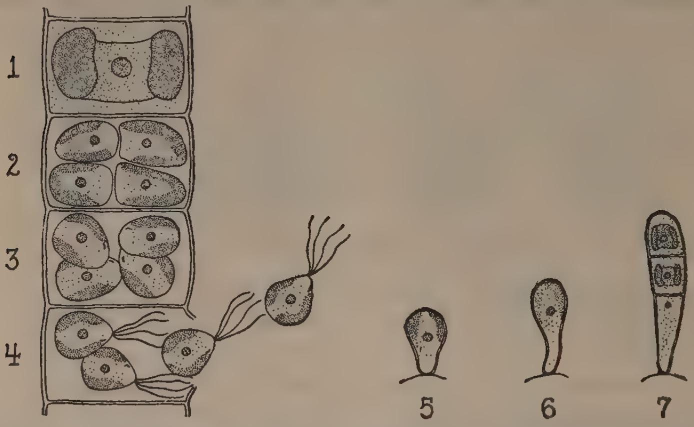


FIG. 117.—Asexual reproduction of Ulothrix, a filamentous green alga. *1*, an ordinary cell of the filament; *2–4*, formation and liberation of zoospores; *5–7*, development of a zoospore into a new filament.

Differentiation of somatic and germ cells.—In unicellular organisms every cell is capable of reproduction, by one or more of the methods described above. The same is true in the simpler colonial forms in which all the cells are alike. But in many species, especially of algae, which form permanent and definite colonies, some of the cells lose the power of reproduction entirely; that is, the cells composing the colony are *differentiated* into two kinds, one of which ceases to divide when the colony has attained its mature form, while the other kind reproduces the colony. The former are called *somatic cells*, the latter *germ cells.*

An interesting series of forms, illustrating successive stages of this differentiation, is afforded by the *Volvocaceae*, a family of free-swimming green algae (Fig. 118). The simplest members of this family are unicellular forms (Chlamydomonas, Sphaerella, etc.), in which every cell is capable of reproduction, by binary fission or sporulation. Then there are a number of simple colonial types (Gonium, Pandorina, Eudorina, etc.) in which the colony consists of 16 or 32 cells. In these forms, each cell forms a new colony by cell divisions, the cells of the young colony remaining attached to each other by a gelatinous substance which they secrete; these young colonies finally escape from the gelatinous envelope of the parent colony. In these colonies, as well as in the unicellular forms, *every cell is a germ cell.* But in the genus *Pleodorina*, there are two kinds of cells in every colony. The species *Pleodorina illinoisensis* has 32 cells, four of which are smaller than the others and do not divide; the other 28 cells produce new colonies as described above. This species therefore has 4 somatic cells and 28 germ cells. Another species, *Pleodorina californica*, has a larger number of cells, approximately half of which are somatic cells; the remaining cells, which are much larger, being germ cells. Finally, in the genus *Volvox* the colonies are very large, containing hundreds or thousands of cells, of which the great majority are somatic cells, the function of producing new colonies being confined to a small number of large germ cells (Fig. 118).

Similar series are found in other families of green algae. The condition in Volvox and other complex colonial, or multicellular, algae is typical of all the higher plants and animals: the great majority of the cells are somatic cells, the function of reproduction of the organism being confined to

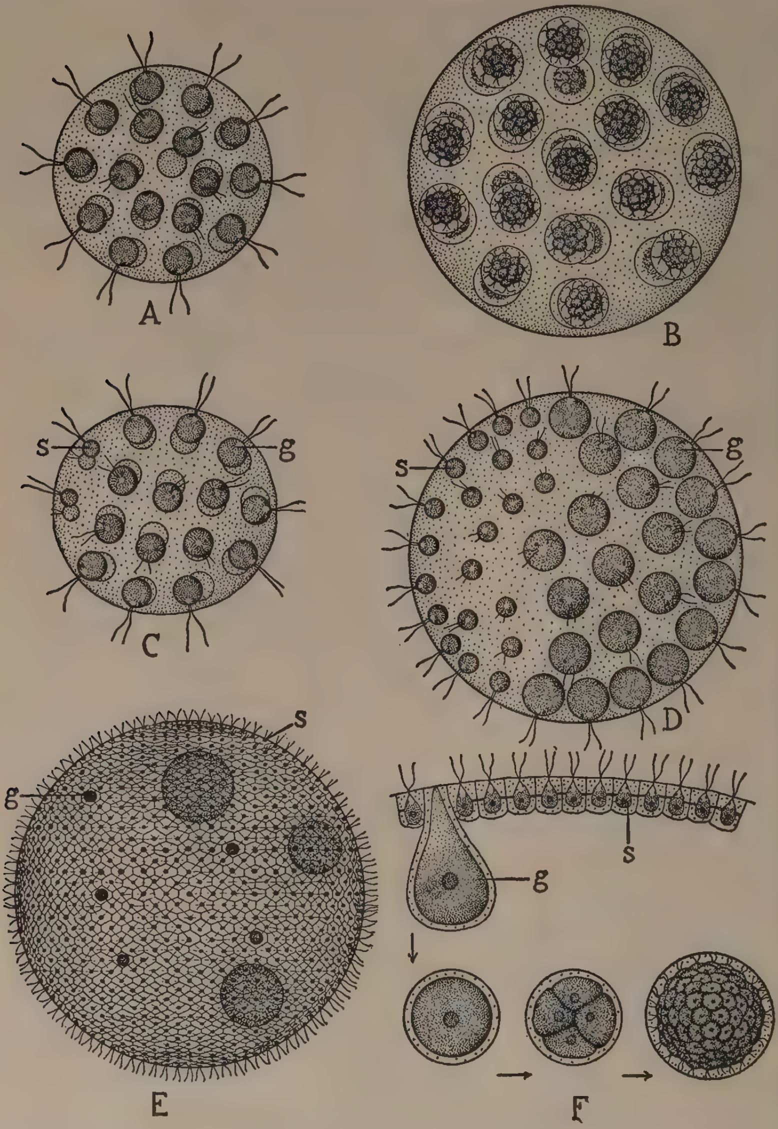


FIG. 118.—Several colonial Volvocaceae. *A*, Eudorina; *B*, the same with young colonies developing by division of the cells of the old colony; in this genus every cell is a germ cell. *C*, Pleodorina illinoisensis; *D*, Pleodorina californica. *E*, Volvox, whole colony, with young colonies developing inside the old one; *F*, small portion of the colony, more highly magnified, and development of germ cell into new colony. *s*, somatic cells; *g*, germ cells.

a relatively few germ cells. The differentiation between somatic and germ cells is the first step in intercellular "division of labor," and may be regarded as marking the transition from "colonial" to "multicellular" organisms (p. 34).

Sexual reproduction.—In some of the simplest organisms asexual reproduction, of the various types described above, is the only mode of reproduction. This is true in all the schizophytes (bacteria and Cyanophyceae), most flagellates, some rhizopods (amoebae, etc.), a few green algae (*e.g.*, Pleurococcus), and some of the fungi. The majority of protozoa and thallophytes, however, exhibit also some form of *sexual reproduction*. The essential feature of this mode of reproduction is the fusion of two cells, or of two nuclei. The two cells participating in this process are called *gametes*. The process of fusion is called *fertilization* or *conjugation*. The cell resulting from fertilization is called a *zygote*.

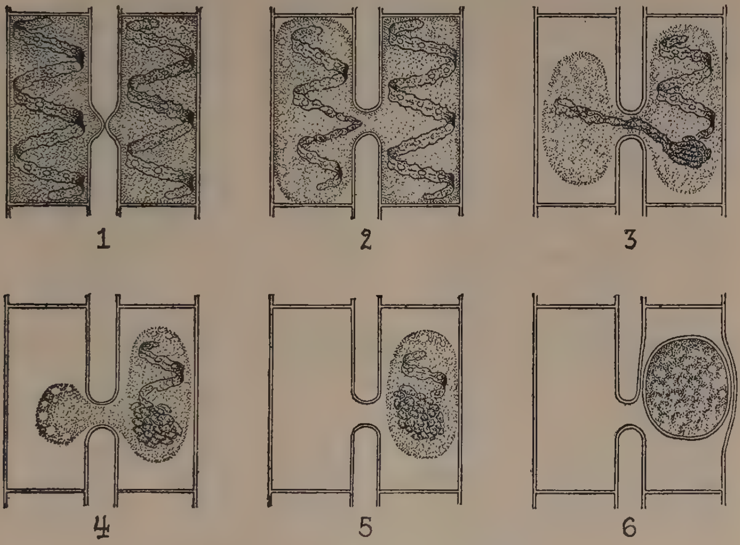


FIG. 119.—Conjugation of Spirogyra.

In some cases, the gametes are the ordinary cells of the organism; *i.e.*, any cell may act as a gamete. This is true in many of the protozoa and in one group of algae, the Conjugatae. The most familiar representative of this group is Spirogyra (Fig. 119). In this plant conjugation may occur between two adjacent cells of the same filament, or between the opposite cells of two filaments lying parallel and close to each other. Short tubes grow out from the gamete cells; these meet and join, the cell wall between them dissolving away (Fig. 119, *1*, *2*). The whole protoplasm of one gamete passes through the connecting tube into the other cell, with which it fuses (Fig. 119, *3–5*). *The nuclei of the two gametes fuse to form the zygote nucleus* (Fig. 122, *1*, *2*): this is the essential act of fertilization. The zygote grows a thick cell wall, and forms a resting spore, called a *zygospore* (Fig. 119, *6*), which is very resistant to freezing or drying. With the return of favorable conditions, the zygospore germinates, forming a new filament by cell divisions. This type of conjugation—complete and permanent fusion of two ordinary cells—is found in all the Conjugatae and also in many protozoa, with various modifications in details.

The ciliates have a peculiar type of conjugation, found in no other organisms. Paramecium is the most familiar representative of this group. At the time of conjugation, two paramecia come together and partially fuse, temporarily, over a small area of their adjacent surfaces. The macronuclei disintegrate and disappear. The micronucleus of each cell divides twice, forming four micronuclei. Three of these degenerate, while the fourth divides again, forming two *gamete nuclei* in each cell. One of the gamete nuclei of each cell passes over into the other cell, where it fuses with the second gamete nucleus of the latter. By this process the two paramecia have reciprocally fertilized each other, and they now separate. The zygote nuclei proceed to divide several times, and give rise to both macronuclei and micronuclei of the cells formed by fission of the exconjugants. This type of conjugation is peculiar in the respect that the gamete cells do not fuse completely; but the essential act of fertilization, *the fusion of two gamete nuclei to form the zygote nucleus*, is the same here as in all other types of sexual reproduction.

In many of the algae (and also in some protozoa), the gametes are not the ordinary cells, but small flagellate cells similar to, or identical with, the zoospores (p. 366). In some cases, the very same cells may act either as asexual zoospores or as gametes. This is illustrated by Ulothrix, a rather simple filamentous green alga. In this plant, the number of zoospores produced by division of one ordinary cell may vary from 4 to 64; the larger the number, the smaller the size of the spores. The larger spores soon settle down and develop new filaments by cell divisions (Fig. 117). The smaller spores *may* also germinate in the same way, but their growth is slower and the filaments produced by them are smaller and less vigorous. More usually, these smaller spores fuse in pairs; *i.e.*, they act as gametes, each pair forming a zygote (Fig. 120). The zygote forms a thick-walled zygospore, as in Spirogyra. Upon germination, however, it does not give rise directly to a new filament, but to another crop of spores, each of which may develop into a filament. The conditions in Ulothrix apparently represent a transition from asexual zoospores to sexual gametes. In many other green algae the gametes are similar to, but smaller than, the asexual zoospores.

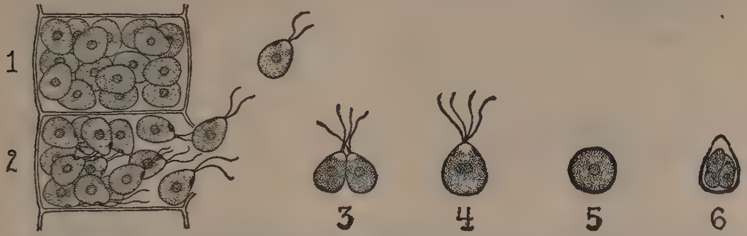


FIG. 120.—Sexual reproduction of Ulothrix. *1*, *2*, formation and liberation of gametes; *3*, *4*, conjugation of gametes; *5*, zygote; *6*, division of zygote into spores (four or more), each of which develops into a new filament (as shown in Fig. 117, *5*–*7*).

In all the types of sexual reproduction described above, the two gametes are exactly alike. Several families of green algae afford interesting series of forms illustrating successive stages from this simple condition to that found in higher organisms, where the two gametes are very unlike in size and form. We may select our illustrations, again, from the Volvocaceae (Fig. 121). All the plants of this family have some type of sexual reproduction, in addition to the asexual methods previously described (p. 367). The unicellular form Chlamydomonas produces gametes similar to, but smaller than, the asexual zoospores; all the gametes are alike in size and form, and apparently any two of them may fuse to form a zygote. The same is true in the simple colonial form Gonium: the gametes are simply the small cells of a young colony, which separate instead of remaining attached as usual (p. 367), and fuse in pairs to form zygotes. In Pandorina the conditions are similar, except that the gametes are of two sizes, and fusion *usually but not always* occurs between a smaller and a larger gamete. In Eudorina, the two kinds of gametes are sharply differentiated in size, though otherwise similar, and fusion *always* occurs between a small one (*microgamete*) and a large one (*macrogamete*). In Pleodorina and Volvox,

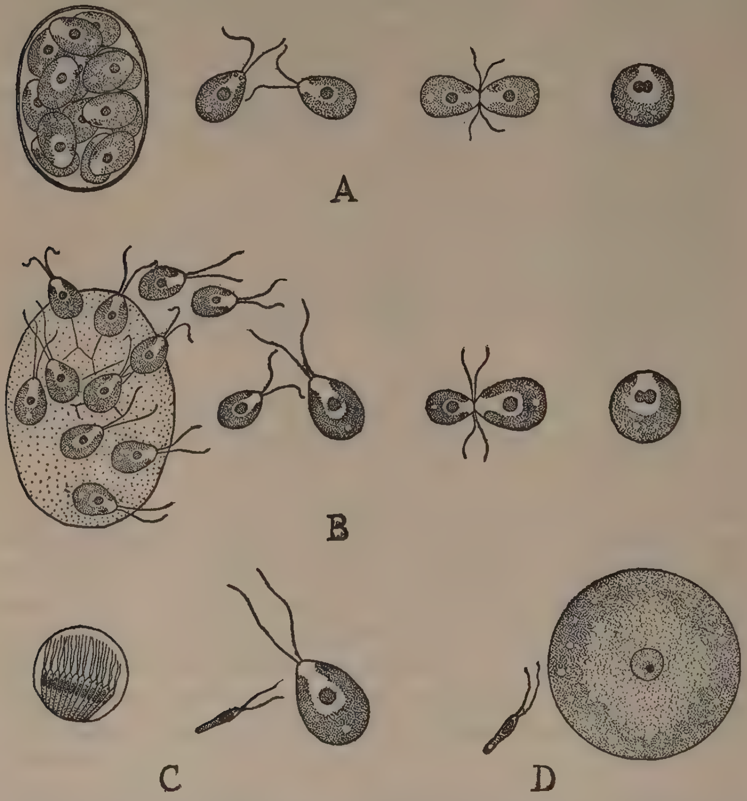


FIG. 121.—Sexual reproduction of several Volvocaceae. *A*, Chlamydomonas: formation of gametes and conjugation of two equal gametes. *B*, Pandorina: liberation of gametes and conjugation of two unequal gametes. *C*, Eudorina: formation of microgametes; a micro- and a macrogamete. *D*, Volvox: a microgamete (sperm-cell) and a macrogamete (egg-cell).

differentiation between the two kinds of gametes is much greater: some of the germ cells, by growth without cell divisions, produce large spherical non-motile macrogametes; others, by many divisions, produce numerous much smaller flagellate microgametes. Fertilization is effected when one of the free-swimming microgametes meets and fuses with a macrogamete. When the gametes show this extreme differentiation, the macrogamete is called an *egg-cell* or *ovum*, the microgamete a *sperm-cell* or *spermatozoon*. These two types of gametes are found in many of the multicellular algae and in *all higher organisms*, both plants[1] and animals. This differentiation represents a "division of labor" between the gametes: the sperm-cell by its motility effects the meeting and fusion of the gametes; the large, non-motile egg-cell contains a large amount of *stored food material* which serves for the nutrition of the zygote during its growth and development. Despite the enormous difference in size of the two gametes, their *chromatin contents are exactly equal;* that is, each contains the same number and kinds of chromosomes (p. 356). Fertilization always involves the fusion of *one sperm-cell nucleus with one egg-cell nucleus.*

In some species of sexually reproducing organisms each multicellular individual produces both sperm-cells and egg-cells; such organisms are called *monoecious.* In other species, some individuals produce only sperm-cells, other individuals only egg-cells; such species are called *dioecious.* The individuals which produce sperm-cells (microgametes) are called *males*, and those which produce egg-cells (macrogametes) *females.* The terms male and female are often applied also to the gametes themselves, the microgametes being called male gametes and the macrogametes female gametes. Both monoecious and dioecious species are found in almost every group of plants and animals, often among closely related species; *e.g.*, some species of the genus Volvox are monoecious, others dioecious. The term *sexual reproduction*, it should be noted, does not necessarily imply the differentiation of two sexes, nor even—as we have seen among some of the simpler organisms—of two kinds of gametes.

Fertilization and reduction; haploidy and diploidy.—It was emphasized in the preceding chapter (p. 356) that all the cells of any one species of organisms ordinarily contain the *same number of chromosomes*, which is maintained by the division of each chromosome at every mitosis. But when two gamete nuclei fuse, at fertilization, the number of chromosomes must obviously be doubled, unless the individual chromosomes fuse also. As a matter of fact, the chromosomes do not fuse at fertilization, and therefore *the zygote nucleus always contains twice as many chromosomes as each gamete nucleus.* Conversely, each gamete nucleus contains half as many chromosomes as the zygote nucleus. Since the number or chromosomes remains the same from generation to generation, there must obviously be a *reduction of the chromosome number* to half of that in the zygote nucleus, at some time between fertilization and the next generation of gametes. The details of this process will be discussed later, in connection with the higher organisms, where it has been more fully studied (p. 411). We may note here, however, that it is always effected by a peculiar kind of mitotic division, in which the individual chromosomes do not split, but half of them go to each pole of the spindle, and therefore each daughter nucleus receives only half the total number. This kind of division is called a *reduction division.* The number of chromosomes in the gamete nucleus is called the *haploid* number; that in the zygote nucleus is called the *diploid* number. If the haploid number of any particular species be n, its diploid number is $2n$.

---

[1] In the seed-plants the microgametes are considerably modified in form (Fig. 145).

Among the organisms discussed in this chapter, the reduction division occurs at various stages of the life cycle. In Spirogyra, for instance, it is one of the first two divisions of the zygote nucleus. Before the zygospore germinates, its nucleus divides twice, forming four nuclei, of which three degenerate while the fourth becomes the functional nucleus (Fig. 122). It is a characteristic phenomenon, in practically all organisms, that at the time of reduction there are two nuclear divisions in rapid succession, and it is very difficult to determine which of these is the true reduction division. It is also characteristic in many, though by no means all, cases that three of these four nuclei degenerate, only one becoming functional. The significance of these phenomena will be discussed later (Chapters XX, XXI). In the zygospore of Spirogyra, the total number of chromosomes seen in the second division is just half of that present in the first, so that the functional nucleus certainly has the haploid number of chromosomes. All the nuclei of the filament cells, which are derived from this nucleus by ordinary mitoses, therefore have the same number; *i.e.*, in this plant all the ordinary, asexually reproducing, cells are *haploid*. This condition prevails in most of the green algae and the fungi which have been studied, in some of the red algae, and also in a few parasitic protozoa.

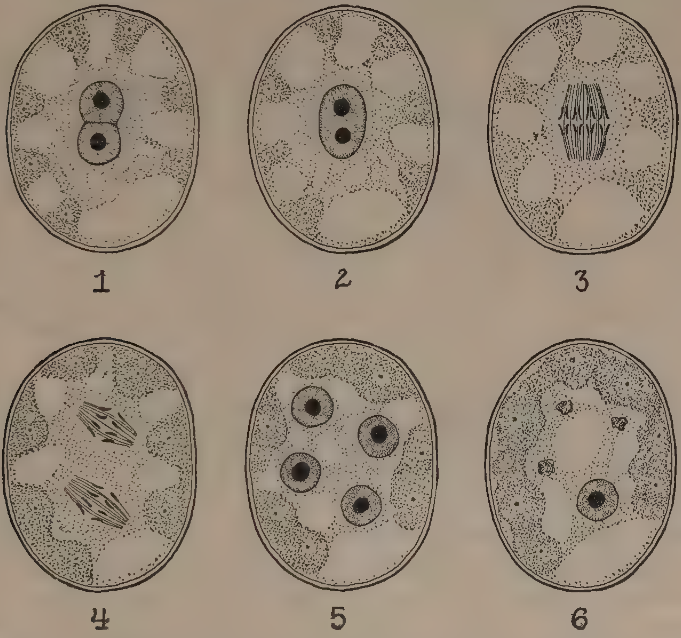


FIG. 122.—Fertilization and reduction in Spirogyra. *1*, *2*, fusion of gamete nuclei to form the zygote nucleus; *3*, first division of the zygote nucleus, with the diploid number of chromosomes; *4*, second nuclear divisions, with the haploid number of chromosomes; *5*, the four haploid nuclei formed by these divisions; *6*, three of these four nuclei degenerating.

In Paramecium, the condition is exactly opposite, in a sense, to that in Spirogyra. Here the ordinary, asexually reproducing, cells are *diploid*. Reduction is effected by one of the first two divisions of the micronucleus during conjugation (p. 370). Here, again, only one of the four haploid nuclei formed is functional, producing by ordinary mitosis the two gamete nuclei. The zygote nucleus has, of course, the diploid number, which it transmits by ordinary mitoses to all its asexual descendants. This condition—the ordinary cells diploid, with reduction just before fertilization—prevails in most of the protozoa which have been studied and in a few algae (*e.g.*, the brown seaweed Fucus and some of the diatoms).

A condition intermediate between these two extremes is found in some of the brown algae and red algae (seaweeds). In these cases, the zygote develops, without reduction, into a *diploid* multicellular plant. This plant produces *spores*, reduction occurring in one of the last two nuclear divisions in spore formation, so that the spores are *haploid*. Each spore develops asexually into a *haploid* multicellular plant, which produces gametes by ordinary mitoses. The gametes fuse to form a zygote, which produces a diploid plant again, and so on. This kind of life cycle is called *alternation of generations*. The haploid, gamete-producing generation is called the *gametophyte;* the diploid, spore-producing generation the *sporophyte*. In some of these seaweeds, the two generations differ markedly in general structure and external appearance; but in other species the two generations appear entirely similar, differing only in the fact that the diploid plant produces asexual spores while the haploid plant produces gametes.

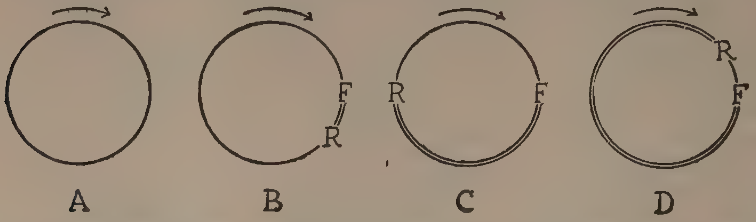


FIG. 123.—Diagrams illustrating the relations of the haploid and diploid stages in various types of life cycles (see text). In each figure the single line represents the haploid, the double line the diploid, condition. The direction of the arrows indicates the succession of cell generations. *F*, fertilization; *R*, reduction.

The relations of the haploid and diploid stages in these various types of life cycles are summarized in the accompanying diagram (Fig. 123). *A* may be assumed to represent the condition in schizophytes and other organisms which have no sexual reproduction, and therefore no fertilization or reduction; though the terms haploid and diploid have here, of course, no real meaning. *B* represents the life cycle of Spirogyra, etc., where reduction follows soon after fertilization, restoring the haploid number. *C* represents the alternation of generations as found in some of the red algae and brown algae, where reduction is postponed until the time of spore formation. Finally, *D* represents the situation in Paramecium, etc., where reduction is still further postponed until shortly before the next fertilization. In some cases, different types of life cycles are found in rather closely related organisms; *e.g.*, among the red algae (*B* and *C*), the brown algae (*C* and *D*), the diatoms (*B* and *D*), etc. Anticipating the following chapters, it may be noted that *all multicellular animals* conform to type *D*, while the *higher plants* (above the thallophytes) show various intermediate conditions *between B* and *D*—that is, they have *alternation of generations*.

From the foregoing, it is evident that we must modify the statement made in the preceding chapter (p. 355) that "the chromosome number is constant for all the cells of an individual organism, and for the cells of all individuals of the same species" to read "for all cells *in corresponding stages of the life cycle* of the species." The reason why the chromosome number is usually an *even* number (p. 356) is simply that in most of the higher organisms a great majority of the cells are diploid.

The significance of sexual reproduction.—The act of fertilization, which is the distinctive feature of sexual reproduction, is not in itself a method of *reproduction* at all, since it does not directly increase the number of individuals or of cells; indeed, it does just the opposite, making one cell out of two. In most cases, however, fertilization is followed, immediately or after a short interval, by an increased rate of cell division. In the case of Ulothrix, it will be recalled (p. 371), the same spores may either develop asexually or may conjugate; but the smaller spores especially, which would develop only slowly and weakly, if at all, asexually, seem to acquire a greatly enhanced vigor by conjugation. Each zygote, moreover, instead of producing only one new filament—as an asexual spore does—produces a new crop of spores, giving rise to several or many new filaments; so that, in the end, the total number of individuals (*i.e.*, filaments) is increased as an indirect result of fertilization. In this plant also, as in most algae, the zygote forms a resistant zygospore, which is able to survive conditions fatal to the ordinary cells. In these organisms, therefore, sexual reproduction also serves as a method of *protection* against unfavorable conditions (freezing in the winter, drying in the summer) and of wider *dispersal* (through the air). It should not be forgotten, however, that other organisms—bacteria, etc. (p. 366)—form resistant spores asexually.

In many of the protozoa—*e.g.*, ciliates—also, conjugation is followed by an increased rate of cell division. But, in some of these organisms at least, the same effect may be produced by changes of environmental conditions. In higher organisms, this effect of fertilization is very striking: the egg-cell is *activated* by the entrance of the sperm, which initiates, usually immediately, a rapid succession of cell divisions leading to the production of a complex multicellular organism. Here again, however, the same effect may be produced by a variety of artificial chemical or physical agents (p. 391).

In short, the process of sexual reproduction seems to increase the *vigor* of the resulting cell—that is, its capacity for growth, cell division, and resistance to injury—thus favoring the survival and multiplication of the species; but the same effects can often be produced by other factors. That sexual reproduction is not *essential* to the continuation of life is proved by the fact that many of the simplest organisms—schizophytes, etc. (p. 369)—have no sexual reproduction at all, continuing to multiply asexually indefinitely—some of them, indeed, at a greater rate than any other organisms. A number of higher plants, also, and even a few multicellular animals, reproduce only by asexual methods, and appear to be able to multiply in this way indefinitely. In recent years it has been found that cells taken from the body of a higher animal and grown in a suitable nutrient solution can continue to grow and multiply indefinitely—long after the animal from which they came would have died of old age. These facts indicate that the capacity for unlimited growth and reproduction by cell division is a property of all living cells, *under favorable external conditions*, without the necessity of fertilization. In many of the lower organisms, and also in the higher plants, sexual reproduction is induced by unfavorable conditions, such as insufficient food supply, and may perhaps be regarded as a process which enables the species to survive such conditions.

Perhaps the greatest significance of sexual reproduction is found in the nuclear phenomena of fertilization and reduction. These processes result, as we shall see later (Chapter XXII), in a mixing and reassortment, in every generation, of the *genes*, since some of the chromosomes brought together by fertilization and separated by reduction may contain qualitatively different genes. This results in increased *variability—i.e.*, individual differences—, which in itself greatly favors the survival and multiplication of the race (Chapter XXV).

CHAPTER XX

REPRODUCTION OF MULTICELLULAR ANIMALS

ALL metazoa (multicellular animals), with very few exceptions, reproduce sexually. Many, though not most, of them have also asexual methods of reproduction. The method of sexual reproduction is essentially the same in all: the fusion of two dissimilar gametes—egg and sperm—to form a unicellular zygote which develops—by growth, cell divisions, and differentiation—into a multicellular animal like the parents. Asexual methods of reproduction, on the other hand, differ widely among various kinds of animals; and many of the higher animals have no form of asexual reproduction.

We shall discuss first the mechanisms and processes of sexual reproduction, as the typical and practically universal mode of reproduction in multicellular animals. Later some of the asexual methods of reproduction in these animals will be described briefly.

Reproductive organs.—The function of reproduction, like other functions in multicellular organisms, is served by specialized organs. The *essential reproductive organs*, in which the gametes are formed, are called the *gonads*. The male gonads, which produce sperm-cells, are called *spermaries* or *testes;* the female gonads, which produce egg-cells, are called *ovaries*. Both monoecious (*hermaphroditic*) species and dioecious species are found in every major group of animals. In some groups monoecious species predominate, but on the whole, especially among the higher animals, there are many more dioecious species. In most monoecious animals the spermaries and ovaries are separate organs; in some species eggs and sperms are produced by the same gonads, but usually not at the same time.

The simplest type of gonads in multicellular animals are those of Hydra, which are merely temporary structures formed at the period of sexual reproduction (Fig. 124). They appear as small swellings on the outer surface of the body, the spermaries near the upper end, the ovaries nearer the foot. These swellings are formed by accumulation of some of the interstitial cells (p. 185) of the ectoderm under the epithelial cells at these points. These interstitial cells are the germ cells (p. 367), which give rise to the gametes. In the spermaries, the germ cells divide many times, forming a large number of small flagellate sperm-cells; eventually the layer of epithelial cells forming the outer wall of the spermary breaks, liberating the sperms into the surrounding water. In the ovary, the germ cells also divide several times, producing a number of amoeboid cells. These cells are "cannibalistic": one finally devours all the others, becoming a large egg-cell. When the egg-cell is mature the epithelial layer covering it breaks away; the egg may now be fertilized by a sperm-cell which, swimming about in the surrounding water, chances to come into contact with it.

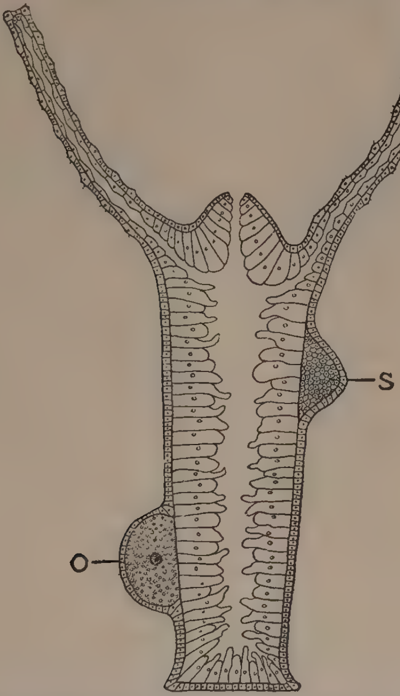


FIG. 124.—Sexually mature Hydra, longitudinal section. *s*, spermary; *o*, ovary.

In most animals the gonads are permanent organs of somewhat more complex structure, but their function is the same—the production of the gametes; they are therefore the essential organs of sexual reproduction. In addition to these, most of the higher animals have various *accessory reproductive organs*, concerned in the liberation of the gametes, in bringing the gametes together to insure fertilization, or in the nutrition and protection of the zygote during the early stages of its development.

In all animals above the coelenterates, the gonads are located inside the body cavity. In some species, the gametes escape through pores in the body wall or by rupture of the body wall. In most animals, however, the gametes reach the exterior through special ducts, the *gonoducts* (*spermiducts* and *oviducts*), which are either attached directly to the gonads or open to the body cavity at their inner ends. Other accessory reproductive organs, usually connected with the gonoducts, include: in the male, glands secreting *seminal fluid* in which the sperm-cells swim, *seminal vesicles* in which the sperms may be stored for a time, *intromittent organs* by which the sperms are introduced into the female, etc.; in the female, glands secreting nutritive substances and protective envelopes or shells about the egg-cells, *sperm receptacles* in which the sperms are stored after mating until fertilization, *uteri* (enlargements of the oviducts) in which the eggs may be stored for a time or the zygotes may pass through their early development, etc. The forms and relations of all these reproductive organs vary greatly in the different groups of animals; in many animals they are more or less intimately connected with the excretory system. The complexity of the reproductive system is not necessarily proportional to that of the general structure of the animal: the flatworms, for instance, which are in most respects the simplest animals above the coelenterates, have reproductive organs at least as complex as any of the higher animals. The reproductive system is often especially complex in monoecious animals (flatworms, earthworms, etc.) because complete male and female systems of reproductive organs occur in each individual.

All vertebrates (with a few exceptions among fishes) are dioecious. In this group the reproductive system is more or less closely connected with the excretory system (more especially in the males), so that the two systems are often called, collectively, the *urino-genital system.* This connection is merely an incidental anatomical association, the functions of the two systems being, of course, entirely different. In the males of almost all vertebrates, the spermiducts are attached to the testes (spermaries), the sperm-cells developing inside the testes and passing directly into the spermiducts. In many of the lower vertebrates (fishes and amphibia), these ducts open into the kidneys, the sperms passing through the urinary tubules and the ureters to the cloaca. In the higher vertebrates the spermiducts have no connection with the kidneys. In reptiles and birds the spermiducts open separately into the cloaca; in mammals, into the urethra (the duct from the urinary bladder to the exterior). In the females of most vertebrates, the oviducts are not attached to the ovaries, the egg-cells being

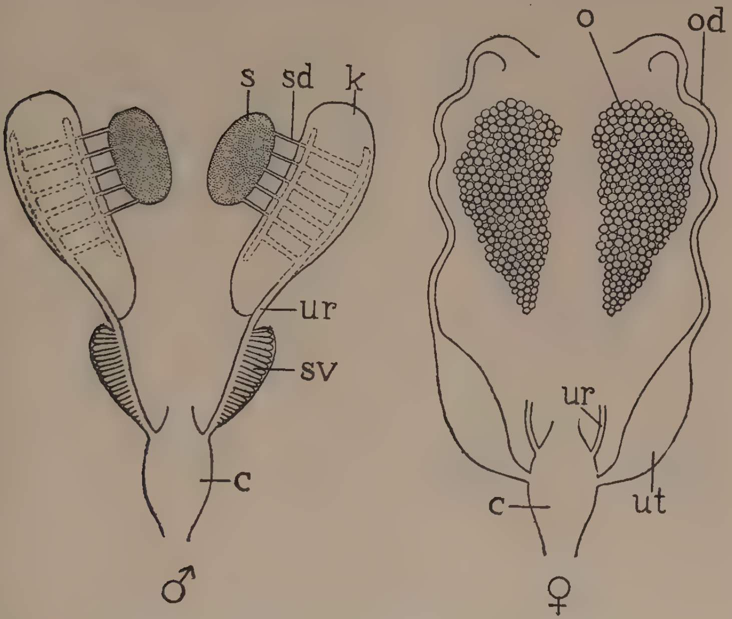


FIG. 125.—Diagrams of reproductive organs of male (♂) and female (♀) frog. *s*, spermary (testis); *sd*, sperm ducts; *k*, kidney (dotted lines show the connections of the sperm ducts with the ureter, within the kidney); *ur*, ureter; *sv*, seminal vesicle; *o*, ovary; *od*, oviduct; *ut*, uterus; *c*, cloaca.

discharged from the surface of the ovaries into the coelom, from which they pass into the open inner ends of the oviducts. The oviducts are not connected with the kidneys or the ureters. In most vertebrates except mammals, the oviducts open separately into the cloaca. In mammals the two oviducts unite, near their outer ends, to form a single passage which opens directly to the exterior in conjunction with, or very close to, the opening of the urethra. The oviducts of most vertebrates are enlarged near their outer ends, forming the uteri; in some mammals there is a single uterus formed by coalescence of the two oviducts.

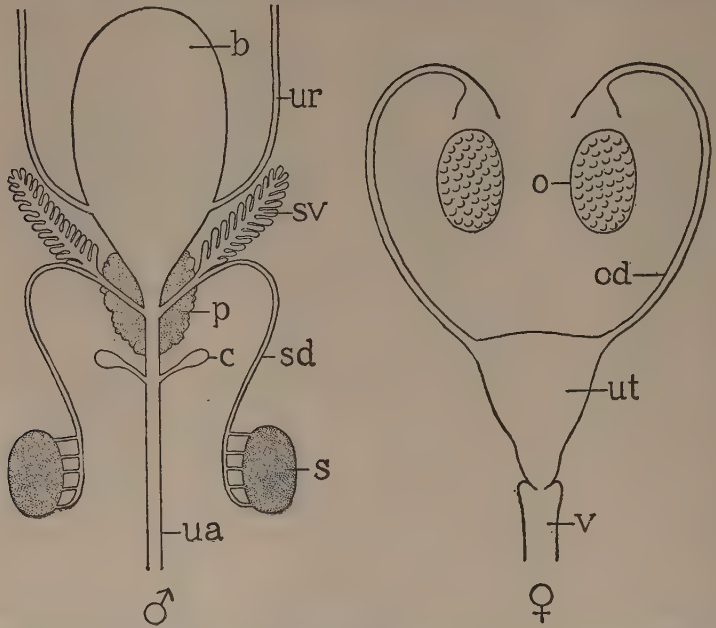


FIG. 126.—Diagrams of reproductive organs of man. *s*, spermary (testis); *sd*, sperm duct; *sv*, seminal vesicle; *ur*, ureter; *b*, urinary bladder; *ua*, urethra; *p*, prostate gland; *c*, Cowper's gland; *o*, ovary; *od*, oviduct; *ut*, uterus; *v*, vagina.

Secondary sexual characters.—In many of the higher animals there are other differences between males and females besides those of the reproductive organs: differences in size, color, external form, structures peculiar to one sex, etc. These differences are called *secondary sexual characters*. Some of these characters have an indirect relation to reproduction; *e.g.*, the mammary glands of female mammals which furnish nutrition for the young, weapons of offense and defense in male animals which may serve in the competition for mates or in protection of the females and young, etc. Many secondary sexual characters, however, seem to be merely incidental by-products of the more fundamental differences between the two sexes. In some cases, especially in the vertebrates, secondary sexual characters are probably due, in part at least, to the action of internal secretions of the gonads (p. 328). In other cases, however, (*e.g.*, in insects), these characters are more direct local effects of the primary hereditary difference between the two sexes, which exists in every cell of the body (Chapter XXII).

The gametes of all metazoa are of two highly specialized types—*egg* and *sperm cells*—which exhibit, in almost every respect, opposite extremes of cell differentiation.

The *egg-cells*, or *ova*, are relatively huge cells, usually the largest cells of the animal body. Among the smallest animal ova are those of mammals and of echinoderms, about 0.1 mm. in diameter; the largest are those of certain birds (ostriches) and fishes (sharks), which may reach a diameter of 8 or 10 cm.[1] The ovum is typically spheroidal, though other forms—ellipsoidal or almost cylindrical—occur in some animals.

The size of egg-cells is determined chiefly by the amount of stored food material, or *yolk*, which they contain. In eggs containing a relatively small amount of yolk, it is distributed more or less uniformly through the cytoplasm (*homolecithal* eggs). In those with more abundant yolk, it is usually concentrated toward the lower side of the cell, leaving the relatively small amount of undifferentiated cytoplasm, and the nucleus, at the upper pole (*telolecithal* eggs). Some eggs (*e.g.*, those of insects) have the yolk in the central region, with most of the undifferentiated cytoplasm in a thin peripheral layer (*centrolecithal* eggs).

Most, if not all, egg-cells are surrounded by a delicate cell membrane, called the *vitelline membrane*, produced by the egg-cell itself. Outside this, there are often other envelopes of various kinds, secreted by the ovum itself, by surrounding cells of the ovary, or by the oviducts or special glands connected with them; *e.g.*, the shell (*chorion*) of insect eggs, the jelly of frogs' eggs, the white and shell of birds' eggs, etc. Some of these are laid down after the egg-cell is fertilized. In some eggs the envelopes (those present before fertilization) are perforated by a minute pore, the *micropyle*, through which the sperm enters.

---

[1] The egg-cell of a bird's egg is what is popularly called the yolk, the white being a non-cellular secretion.

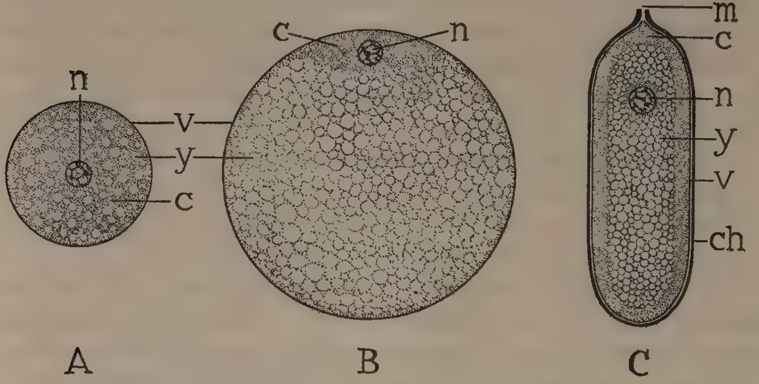


FIG. 127.—Diagrammatic vertical sections of egg-cells: *A*, homolecithal egg; *B*, telolecithal egg; *C*, centrolecithal egg of an insect. *n*, nucleus; *c*, cytoplasm; *y*, yolk; *v*, vitelline membrane; *ch*, chorion (shell); *m*, micropyle.

The *sperm-cells*, or *spermatozoa*, of different species of animals exhibit a great variety of size, form, and structure. Those of most animals are elongate, uni-flagellate cells, though bi-flagellate and non-flagellate forms occur in several groups of invertebrates. The most common form consists of a relatively thick *head* and a long slender flagellum or *tail*. The dimensions of the head are usually between 0.001 and 0.01 mm.; the tail is much longer but very slender, so that the total volume of the sperm-cell is always less than a thousandth, often less than a millionth, of that of the egg-cell. The number of sperm-cells is correspondingly greater, being commonly millions of times more numerous than the eggs. This great excess of sperms increases the chances of fertilization of the eggs, as only *one sperm* is necessary to fertilize each egg.

The *head* of the sperm-cell displays a great diversity of shape in different species and groups of animals. The main bulk of the head is constituted by the *nucleus*, which occupies all but the anterior tip of the head. The nucleus usually consists of a solid mass of *chromatin*, covered by a very thin membrane. In most cases, this chromatin constitutes much the greater part of the total volume of the sperm-cell; despite the enormous difference in size of the sperm and egg cells, and even of their nuclei, *the amount of chromatin is the same in both gametes.* The anterior tip of the head is usually occupied by a cytoplasmic structure called the *acrosome*, usually much smaller than the nucleus. At the posterior end of the head there is often a small cytoplastic *middle-piece*, of various shapes, connecting the head with the tail. The *tail*, or flagellum, consists of a contractile *axial filament* surrounded by a very thin cytoplasmic sheath which does not extend to the extreme tip of the flagellum.

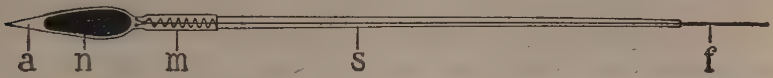


FIG. 128.—Diagram of a typical animal sperm-cell. *a*, acrosome; *n*, nucleus; *m*, middle piece; *s*, sheath of flagellum; *f*, axial filament. (Adapted from Wilson.)

The sperm swims, head forward, by whip-like lashings of the flagellum.

Breeding habits.—The activities connected with reproduction are commonly called *breeding habits*, although they are not really habits, in the strict sense of the word (p. 343), but purely reflex or instinctive responses. These activities are largely concerned with bringing the two kinds of gametes into proximity, preliminary to fertilization.

Some monoecious animals are normally *self-fertilizing*, *i.e.*, the egg-cells are fertilized by sperms of the same individual; in such animals the eggs are usually fertilized inside the body. Most monoecious animals, however, are normally *cross-fertilizing*, eggs of one individual being fertilized by sperms from another one. In many of these animals, the two kinds of gametes are not produced in the same individual at the same time. In some cases, the sperms are actually incapable of fertilizing eggs of the same individual. Cross-fertilizing hermaphrodites exhibit, in general, the same varieties of breeding habits as dioecious animals.

Many aquatic animals, especially invertebrates, simply discharge the gametes into the water, where they come together only by chance. This entails, of course, an enormous waste of gametes which never meet opposite ones of the same species, but these animals produce enormous numbers of gametes, so that the small proportion which do happen to meet is sufficient to perpetuate the species. In other aquatic animals the chance of fertilization is increased by congregation of the sexes at the breeding season; *i.e.*, the males and females approach each other and liberate the sperm and egg cells in proximity. In many of the aquatic vertebrates—fishes and amphibia—the meeting of the gametes is further insured by a clasping reflex: the male clasps the female and the seminal fluid containing the sperms is poured over the eggs as they are discharged.

All the preceding breeding methods are obviously possible only in animals which live, or at least breed, in the water, where the gametes are capable of living for some time. In animals which breed on land, the sperm-cells are always introduced into the body of the female; this act is called *copulation.* The organs and methods of copulation vary greatly in different groups of animals; but all land-breeding animals, and also a number of aquatic animals, exhibit some form of copulation. In some cases the sperms are introduced into sperm receptacles in the female which have no connection with the oviducts; from these receptacles the sperms are liberated later, simultaneously with the emission of the eggs, and fertilization occurs outside the body, as in the preceding types. In the earthworms, which breed in this way, the transfer of sperms is reciprocal, as these animals are monoecious: each of the two copulating individuals transfers sperms to the sperm receptacles of the other; later, each worm secretes a cocoon containing a nutritive fluid, into which it discharges its own eggs and the sperms from its receptacles (*i.e.*, the sperms of the other worm), fertilization occurring in the cocoon.

In all the higher vertebrates (reptiles, birds, and mammals), in the insects, and in a number of other animals (some parasitic worms, snails, fishes, etc.), fertilization is *internal*, occurring in some part of the oviducts after copulation. In the vertebrates fertilization usually occurs shortly after copulation. In insects the sperms are stored after copulation in sperm receptacles connected with the oviducts, and fertilization may occur considerably later. In some insects, such as ants and bees, copulation occurs only once in a lifetime, and the sperms may fertilize eggs for years thereafter.

In all cases of external fertilization, the development of the zygote after fertilization is also external; *i.e.*, outside the body of the mother. Most animals with internal fertilization lay their eggs soon after fertilization (birds, most insects, etc.); in these cases also, the development of the zygote is external. But in most mammals and a few other animals (some insects, fishes, reptiles, etc.), the zygotes are retained within the uteri of the mother until they have attained an advanced stage in their development. Animals which lay their eggs, either before or shortly after fertilization, are called *oviparous;* those which give birth to well-developed young are called *viviparous.*

Fertilization.—The actual contact of the sperm with the egg seems to occur purely by chance, favored, of course, by the enormous number of sperms and the various mechanisms, described above, for discharging them in proximity to the eggs. Contact of the sperm with the surface of the egg calls forth an instantaneous response of the egg cytoplasm at the point of contact, by which the sperm is engulfed and drawn into the egg. Simultaneously with this local response, the vitelline membrane of the egg separates from the underlying protoplasm over the whole surface, forming the *fertilization membrane.* These visible responses of the egg-cell are accompanied by all the usual phenomena of excitation (p. 238): increased permeability, electrical response, production of lactic acid, and greatly increased oxygen consumption and heat production.

In some cases only the sperm head actually enters the egg, in other cases the whole sperm-cell enters, but the acrosome, middle-piece, and flagellum sooner or later disintegrate and disappear in the egg cytoplasm. The sperm nucleus slowly enlarges, by absorption of fluid from the surrounding egg cytoplasm, until it attains the same size and form as the egg nucleus. At the same time, the sperm and egg nuclei approach each other and finally unite, forming the zygote nucleus. In most animal eggs, a large aster is formed in the egg cytoplasm in the vicinity of the sperm soon after its entrance, and moves toward the center of the egg in advance of the sperm nucleus. Sooner or later (either before or after the union of the gamete nuclei) this single aster is replaced by two asters, which assume positions on

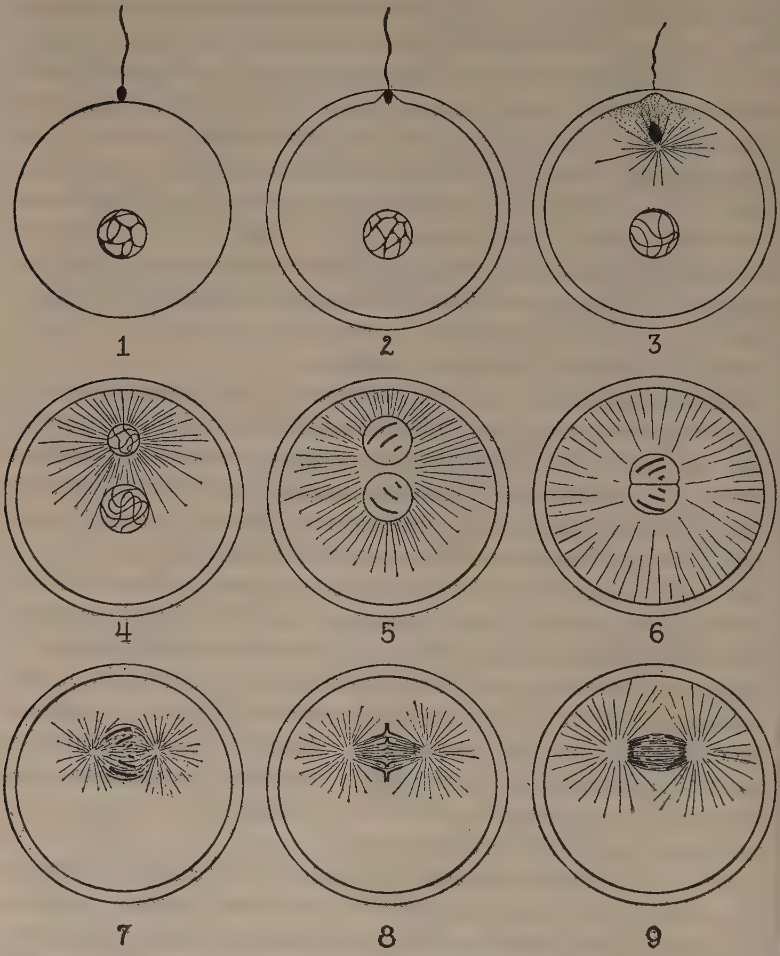


FIG. 129.—Diagram of fertilization. *1*, contact of sperm with surface of egg. *2*, response of the egg: formation of the entrance cone, which engulfs the sperm, and of the fertilization membrane. *3*, sperm head drawn into the egg; appearance of aster. *4*, *5*, enlargement of sperm nucleus and approach of the two gamete nuclei; appearance of the haploid number of chromosomes (here three) in each gamete nucleus. *6*, union of the two gamete nuclei. *7–9*, first division of the zygote nucleus, each daughter nucleus receiving one-half of each chromosome of both gametes.

each side of the zygote nucleus. The zygote now undergoes a typical mitotic division, beginning its development into a multicellular animal.

In many eggs, the prophases of this first mitosis begin in the sperm and egg nuclei before their actual union, so that their chromosomes can be seen and counted separately before they intermingle. In such cases, it can be clearly seen that *each gamete nucleus has the haploid number of chromosomes*, *i.e.*, half the number present in the ordinary cells of the species (p. 374). In cases where the individual chromosomes can be distinguished by differences of size or shape, each gamete nucleus can be seen to have a similar set of chromosomes, *i.e.*, one of each kind. The *diploid* group of chromosomes in the *zygote* nucleus, formed by the addition of these two haploid groups, therefore consists of *two* of each kind of chromosomes, one of the two coming from each of the gamete nuclei. Each of these chromosomes splits longitudinally and the daughter halves are distributed in the usual way (p. 352). Each of the daughter cells of the zygote therefore contains the whole diploid number of chromosomes, derived from the two haploid sets of the gamete nuclei. As all the cells of the animal are derived from the zygote by mitotic division, they all contain the same number and kinds of chromosomes; therefore *every cell of the body contains an equal number of chromosomes derived originally from each of the two parents.* These facts, though directly observable only in certain favorable cases, are proved even more certainly by other kinds of evidence to be true in all diploid organisms (Chapter XXII).

The process of fertilization, as described above, really comprises two separable events: the response of the egg-cell —formation of the fertilization membrane, cell division, etc. —called *activation;* and the union of the two gamete nuclei, which constitutes *fertilization* proper (p. 369). The activation of the egg, leading to its development, can be brought about in a variety of ways without fertilization. *Artificial activation* of various kinds of eggs can be effected by many chemical substances (fatty acids, carbon dioxide, ammonia, etc.), by increased osmotic pressure (hypertonic solutions), by temperature changes, electrical stimuli, shaking, pricking with a needle, etc., different stimuli being effective with different kinds of eggs. When so activated, the egg forms a fertilization membrane, divides, and develops more or less normally; under favorable conditions, artifically activated eggs have developed into adult animals (frogs, starfish, sea-urchins). Eggs may also be activated by sperms which are incapable of true fertilization; *e.g.*, sperms of a very different kind of animal, or sperms whose nuclei have been killed by radium treatment. These facts indicate that the egg-cell, like any other type of cell, simply gives its own special response to *any effective stimulus* (p. 242). The special response of the egg-cell is what we call its activation, which initiates its development into a multicellular organism. Under natural conditions, the effective stimulus, in most cases, is supplied by the sperm; but in some kinds of animals eggs develop naturally in the entire absence of sperms (p. 415). The essential significance of fertilization, as such, seems therefore to be not the activation of the egg but the union of two nuclei (p. 379).

True fertilization (union of gamete nuclei) can only be effected by a sperm of the same species or a closely related species. In most kinds of eggs, only one sperm normally enters each egg; some kind of change occurs in the egg cytoplasm immediately after entrance of one sperm which prevents the entrance of other sperms. In some kinds of eggs, chiefly those with a large amount of yolk, several sperms normally enter each egg, but in every case *only one sperm nucleus fuses with the egg nucleus.* Occasional exceptions to this rule always result in failure of development or very abnormal development.

Development of the zygote.—The transformation of the unicellular zygote (fertilized egg-cell) into an adult multicellular animal involves a complex series of changes, including cell divisions, differentiation, and growth, which are called collectively its *development.* The zygote from the time of fertilization to the time of hatching or birth—*i.e.*, until its emergence from the egg membrane or shell or the uterus of the mother—is called an *embryo.* The stage of development attained before hatching or birth varies greatly in different kinds of animals, depending chiefly on the provisions for nutrition of the embryo (p. 401). There is no significant distinction, so far as the process of development is concerned, between the embryonic and the post-embryonic stages; the development of the zygote is essentially a continuous process from fertilization to the adult animal.

This process differs in detail in every species of animals; the structural differences of the adult animals are, indeed, the direct results of differences in development. Nevertheless, in some of the broader features, especially in the early stages, of development there are certain fundamental resemblances throughout the whole group of metazoa.

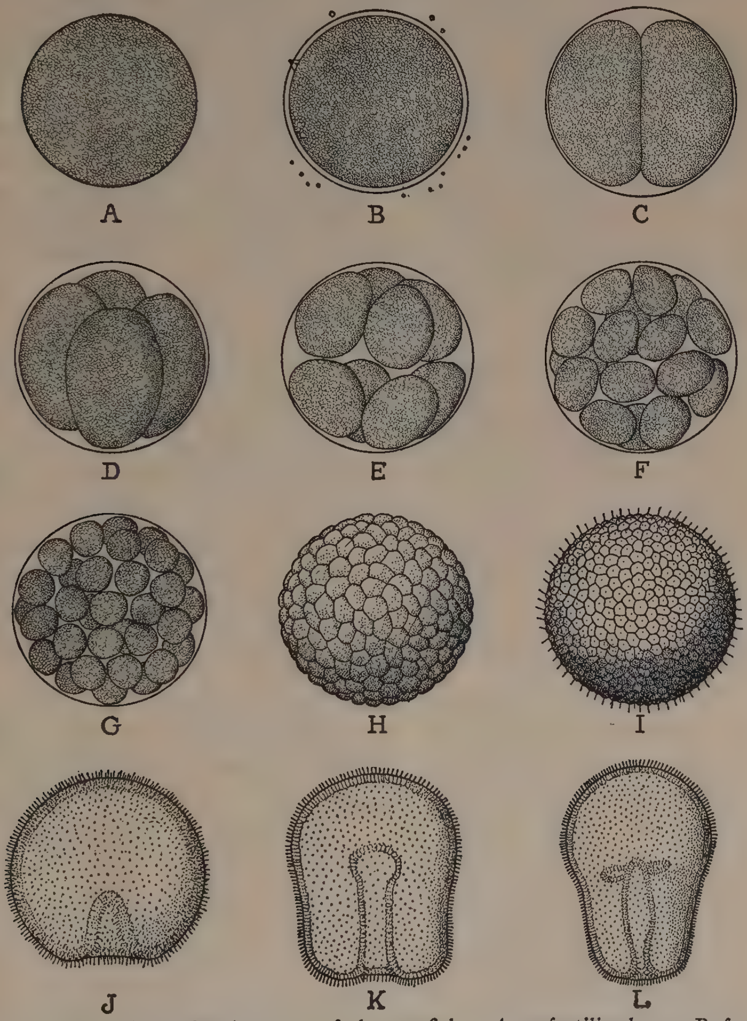


FIG. 130.—Early development of the starfish. *A*, unfertilized egg; *B*, fertilized egg; *C-G*, cleavage; *H*, *I*, blastulae; *J*, *K*, gastrulation; *L*, formation of coelomic pouches.

The development of the zygote begins, soon after fertilization, with a series of mitotic divisions, by which it is divided into a group of smaller cells: this process is called *cleavage*. The form of the cleavage divisions is determined largely by the amount and distribution of the yolk in the egg-cell. In homolecithal eggs, with relatively little yolk (*e.g.*, those of starfish), the cleavage divisions are usually quite regular and approximately equal, so that the number of cells increases in regular geometrical progression—2, 4, 8, 16, and so on—up to several hundred cells, all equal or nearly equal in size. During this process there is no increase in the total size of the embryo, as no food is being taken in from outside. The metabolism of the embryo is carried on at the expense of food substances present in the egg-cell before fertilization, so that the total amount of organic matter in the embryo actually decreases. The whole group of cells formed by cleavage remains enclosed by the original fertilization membrane of the egg. As the cells are formed they tend to round up as much as possible; an intercellular cavity is thus formed in the center of the embryo. This cavity increases in size during the progress of cleavage, and the embryo assumes the form of a hollow sphere of cells surrounding a large central cavity filled with non-cellular fluid. The embryo in this stage is called a *blastula;* its cavity is called the *blastocoel.*

In telolecithal eggs, the cleavage divisions are less regular. The horizontal divisions are always unequal, forming smaller cells above and larger ones below; the lower cells, containing most of the yolk, also divide less rapidly than the upper ones. The blastula, in consequence, is composed of numerous small cells in its upper hemisphere and fewer, larger cells in the lower hemisphere. The blastocoel also is eccentric in position, *i.e.*, nearer the upper pole, and relatively smaller than in the homolecithal type. In general, the greater the amount of yolk in the egg, the more do the cleavage divisions and the form of the blastula depart from the simple symmetrical type. In extreme telolecithal eggs, with a very large amount of yolk (*e.g.*, those of birds, fishes, etc.), the cleavage divisions are confined entirely to the upper surface of the egg cell; the blastula consists of a relatively small disc of cells on the upper surface, roofing over a small flat blastocoel, with a large undivided mass of yolk below. Without going further into the details of cleavage in various types of eggs, we may say that in all metazoa the cleavage of the zygote results in a form of embryo which can be recognized as a blastula, despite its various differences in form in particular cases.

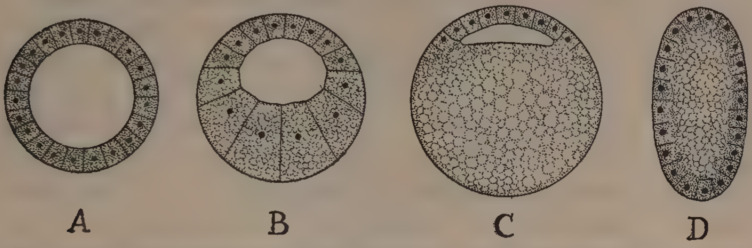


FIG. 131.—Diagrammatic vertical sections of several types of blastulae: *A*, from homolecithal egg; *B*, from moderately telolecithal egg; *C*, from extreme telolecithal egg; *D*, from centrolecithal egg.

The next stage in development is a process called *gastrulation*. This process differs considerably in different animals, depending largely on the form of the blastula. In the simple symmetrical type of blastula, gastrulation is usually effected by invagination of one side of the blastula; *i.e.*, this region is turned inward, much as a hollow rubber ball might be indented by pushing inward at one point (Fig. 130, *J*). By this process the blastocoel is partially—in some cases almost entirely—obliterated, and the embryo assumes the form of a two-layered sac enclosing a new cavity. The embryo in this stage is called a *gastrula*. The new cavity formed by gastrulation is the *enteron;* the inner layer of cells is the *endoderm*, and the outer layer the *ectoderm*. The opening from the enteron to the outside, at the point of invagination, is called the *blastopore;* this opening becomes smaller as the process of invagination is completed. In some animals (*e.g.*, earthworms) the blastopore becomes the mouth; in others (*e.g.*, starfish) it becomes the anus; in many animals, including the vertebrates, the blastopore eventually closes completely and both mouth and anus are formed later.

In embryos with much yolk and small blastocoel, the process of gastrulation is modified in various ways. Despite these differences, we can recognize, in the development of every metazoan animal, a gastrula stage, *i.e.*, a "two-layered" embryo enclosing the enteron or digestive cavity. The two lowest groups of metazoa—the sponges and coelenterates—retain this type of structure throughout life, their adult forms being essentially slightly modified gastrulae (p. 184).

In all animals above the coelenterates, a third layer is formed, shortly after or even during gastrulation, between the ectoderm and the endoderm; this is the *mesoderm*, which gives rise to the greatest part of the tissues of these animals. The method of formation of the mesoderm differs greatly in different groups of animals. In the starfish, the mesoderm is derived chiefly from two hollow pouches which grow out from the enteron, soon after gastrulation, into the space between ectoderm and endoderm (Fig. 130, *L*). These pouches soon sever their connection with the enteron, and eventually grow completely around it; their cavities form the *coelom* and their walls form most of the mesoderm. This method of mesoderm and coelom formation, from diverticula of the enteron, is found in several groups of invertebrates and, in somewhat modified form, in the vertebrates (p. 400).

A more common method of mesoderm formation among the invertebrates is typified by the earthworm. Here the mesoderm originates from two large cells, the *pole cells*, which can be distinguished even in the blastula. During, or somewhat before, gastrulation these cells sink into the blastocoel; their position marks the posterior end of the embryo. The mesoderm is formed by continued division of the pole cells, forming two bands of tissue which grow forward, one on each side of the enteron; later they grow upward and downward around the enteron, completely surrounding it. The coelom originates by separation of the mesoderm cells, forming a series of paired cavities, each pair corresponding to one segment of the adult worm. Eventually the two cavities of each pair meet above and below the enteron. The inner layer of mesoderm, together with the endoderm, forms the wall of the enteron; the outer layer, together with the ectoderm, forms the body wall. The thin layers of mesoderm separating the successive coelomic cavities form the transverse septa between segments seen in the adult worm (p. 191).

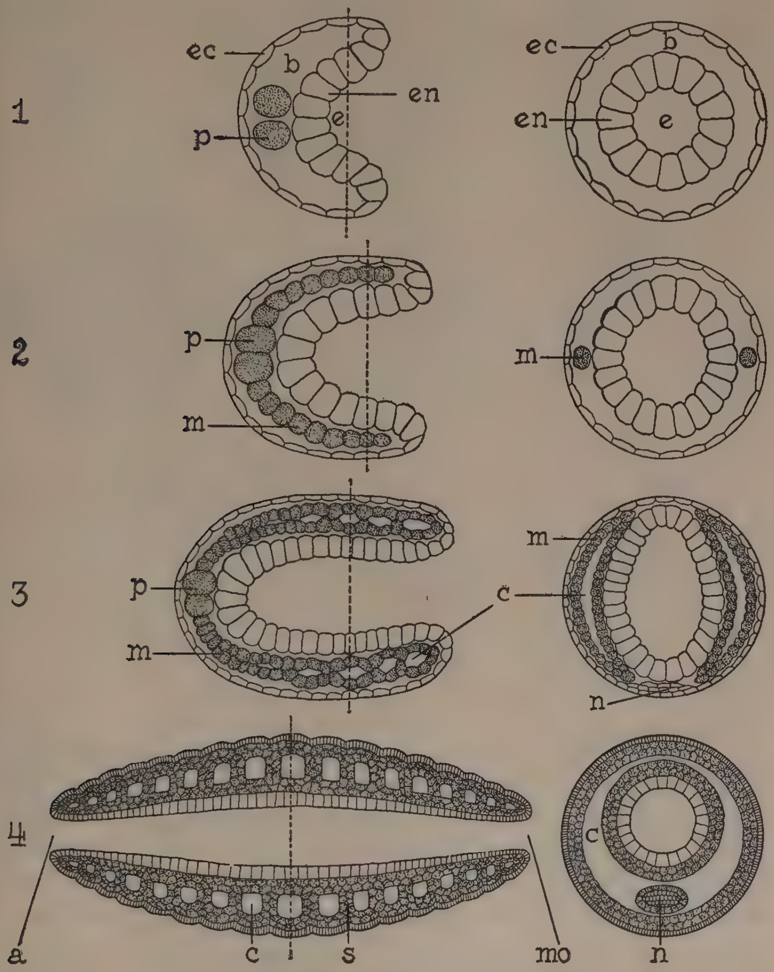


FIG. 132.—Diagrams showing development of mesoderm, coelom, and nerve cord in the earthworm. The figures on the left represent horizontal longitudinal sections, those on the right cross-sections through the points indicated by the dotted lines. *1*, gastrula; *2*, formation of mesoderm from the pole cells; *3*, formation of coelomic cavities, and origin of the nerve cord from the ectoderm; *4*, the general form and structure of the body established; the nerve cord has become separated from the epidermis by the surrounding mesodermal tissue. *ec*, ectoderm; *en*, endoderm; *p*, pole cell; *b*, blastocoel; *e*, enteron; *m*, mesoderm; *c*, coelom; *n*, nerve cord; *a*, anus; *mo*, mouth; *s*, septum. (Adapted, in part, from Sedgwick and Wilson.)

The tissues and organs derived from the respective embryonic layers are, in a general way, identical throughout the metazoa. In the "two-layered" animals (sponges and coelenterates) the ectoderm forms the outer layer, whose functions are chiefly protective and responsive, and the endoderm the inner layer, whose special functions are digestion and absorption of food (p. 186). In the "three-layered" animals (*i.e.*, all those above the coelenterates), the ectoderm forms chiefly the epidermis (outer skin), the sense organs, and the entire nervous system. The nervous system, though very different in form and position in various groups of animals, always originates by thickenings and ingrowths of the ectoderm; in most cases it separates later from the epidermis and becomes surrounded by mesodermal tissues (connective tissue, muscles, etc.). The endoderm forms chiefly the epithelial lining (mucous membrane) of the enteron and its appendages; *i.e.*, of the digestive organs and glands (stomach, intestine, liver, pancreas, etc.), lungs and urinary bladder of higher vertebrates, etc. The mesoderm forms the great bulk of the tissues and organs: the muscles, connective tissues, internal skeleton (cartilage and bone), the circulatory system and blood, the excretory and reproductive organs.

The details of development of the various organs and tissues differ in every group of animals and, in the later stages, in every species. We shall merely describe briefly some of the general features of organogeny (the formation of organs) in the vertebrates. Certain characteristic vertebrate structures begin to appear immediately after, or even during, gastrulation. On one side of the embryo the ectoderm is raised up into two longitudinal ridges, the *neural folds*, including between them a depression, the *neural groove*. These structures mark the dorsal side of the embryo and its longitudinal axis. From the posterior end of the embryo, marked by the location of the blastopore, the neural folds extend forward approximately parallel for some distance but diverging at the anterior end. The neural groove gradually sinks inward until the two neural folds meet and fuse above it, forming a hollow tube of ectoderm, the *neural tube*, which becomes detached from the rest of the ectoderm and eventually sinks entirely below the surface of the embryo. This tube develops into the *central nervous system*, which thus comes to have the form, in all vertebrates, of a longitudinal hollow tube on the dorsal side of

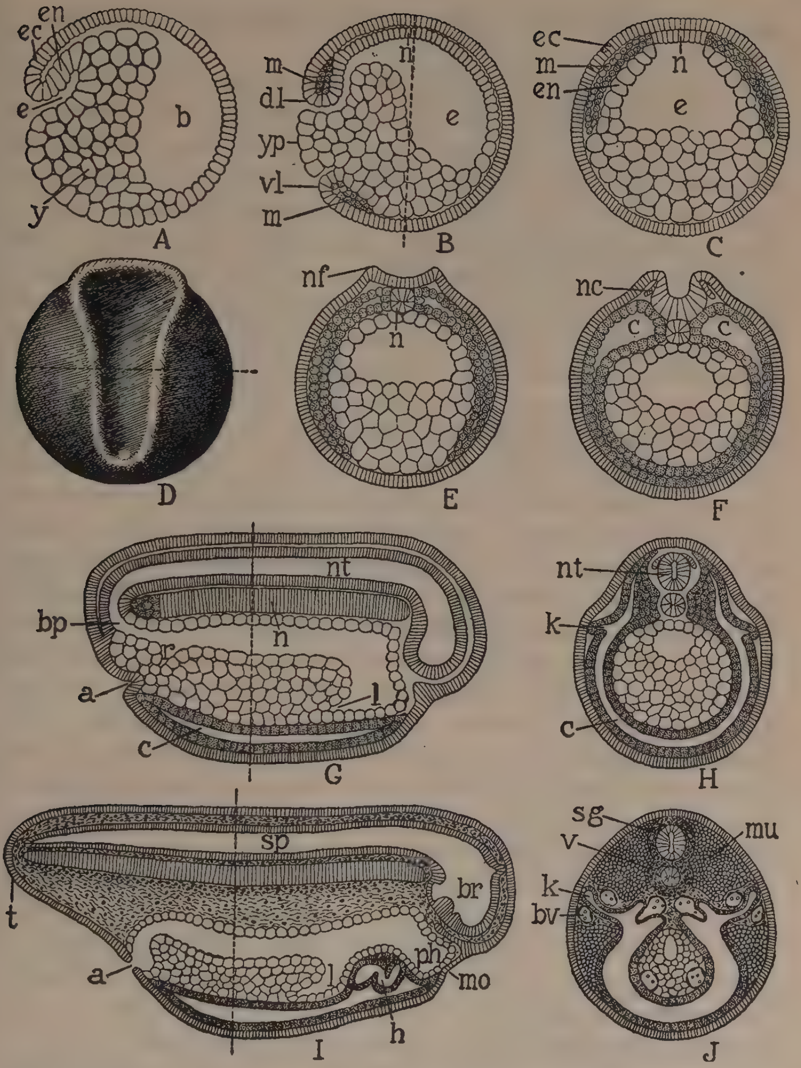


FIG. 133.—Diagrams of amphibian embryos, showing development of typical vertebrate structures. *A*, median longitudinal section of early gastrula; *B*, similar section of late gastrula; *C*, cross-section of same stage (through dotted line in *B*); *D*, surface view of slightly later stage, from the dorsal side, showing neural folds; *E*, cross-section of same stage (through dotted line in *D*); *F*, similar section of later stage; *G*, median longitudinal section of embryo after closing of the neural tube; *H*, cross-section of same stage (through dotted line in *G*); *I*, longitudinal section of embryo at about the time of hatching; *J*, cross-section of same stage (through dotted line in *I*). *ec*, ectoderm; *en*, endoderm; *y*, yolk cells; *b*, blastocoel; *e*, enteron; *m*, mesoderm; *dl*, dorsal lip of the blastopore; *vl*, ventral lip of the blastopore; *yp*, yolk plug; *n*, notochord; *nf*, neural fold; *nc*, neural crest (which develops into the sensory ganglia); *c*, coelom; *nt*, neural tube; *bp*, blastopore; *a*, anus; *r*, rectum; *l*, liver; *k*, embryonic kidney tubule; *br*, brain; *sp*, spinal cord; *t*, tail; *h*, heart; *ph*, pharynx; *mo*, mouth; *mu*, muscle; *sg*, sensory ganglion; *v*, vertebra; *bv*, blood vessel.

the body; its wider anterior portion becomes the *brain*, the remainder the *spinal cord*. At its posterior end the neural tube encloses the blastopore, which thus forms an opening from the neural tube to the enteron; this opening closes later.

At the same time another characteristic vertebrate structure is developing internally. Just below the neural tube, along the mid-dorsal line of the enteron, is formed a longitudinal solid rod of cells, the *notochord*, about which is later developed the *vertebral column* (backbone), the central feature of the vertebrate skeleton. The mesoderm originates partly around the blastopore, where ectoderm and endoderm meet, partly from the dorso-lateral walls of the enteron on both sides of the notochord. It grows upward around the notochord and the neural tube, and downward around the enteron, eventually surrounding each of these structures completely. The mesoderm immediately about the notochord forms the *vertebrae;* that about the neural tube forms the dorsal arches of the vertebrae, surrounding the spinal cord, and the bones of the *cranium*, surrounding the brain. The more lateral portions of the mesoderm form the muscles and bones of the body wall and limbs. The coelom originates by separation of the mesoderm, in the lateral and ventral regions, into two layers; the cavity thus formed is continuous lengthwise and below the enteron, forming a single unsegmented body cavity. On the dorsal side this cavity never quite surrounds the enteron, which thus remains attached to the dorsal body wall by a thin sheet of tissue, the *mesentery* (Fig. 62). The inner layer of mesoderm, next to the endoderm, forms most of the tissues —muscles, connective tissue, etc.—of the wall of the enteron; the outer layer those of the body wall.

The *anus* is formed just below the blastopore, and the *mouth* at the other end of the embryo, by invaginations of the ectoderm which meet and fuse with outgrowths of the enteron. In a similar manner, the *gill slits* (usually five pairs) are formed at the sides of the pharynx in the embryos of all vertebrates; in the higher vertebrates they close again later, except the first pair, which form the Eustachian tubes from the pharynx to the tympanic cavity of the ear (p. 286). The *liver* and *pancreas* are formed by outgrowths from the enteron, which become complexly branched and end in secretory tubules (p. 275). The gland cells of these organs, as well as those of the smaller digestive glands, are all formed from endoderm; their connective tissues, blood vessels, etc., from the surrounding mesoderm. In a similar manner, the *lungs* are formed in the higher vertebrates by an outgrowth from the ventral side of the pharynx; and the *urinary bladder* from the ventral side of the cloaca (in most mammals the urinary bladder later loses its connection with the enteron).

The *nerves* and *peripheral ganglia* are formed by outgrowths from the central nervous system. The *sense organs* are formed by ingrowths from the surface ectoderm or outgrowths from the central nervous system, or both.

The *blood vessels*, including the heart, and the *lymphatic vessels* originate as fissures among the mesoderm cells, which eventually communicate with each other to form a continuous system of vessels. *Blood cells* (red and white corpuscles) are formed, in the embryo, from cells originally included in the cavities of these vessels, or from the walls of the vessels; later, they are formed in special tissues—bone marrow, lymphatic tissue, etc. (p. 210). The *urinary tubules* of the kidneys, the *ureters*, and the *gonoducts* are formed from the mesoderm of the outer (body wall) layer in a manner essentially similar to that of the blood vessels. The *gonads* are formed by outgrowths of this same layer into the coelom. The history of the *germ cells* will be described later (p. 408).

Nutrition of the embryo.—Throughout the course of development, the cells of the embryo are carrying on very active metabolism: destructive metabolism liberating the energy manifested in cell divisions, movements of cells and tissues, etc.; and constructive metabolism synthesizing the special components of nuclei, cytoplasmic and intercellular structures, etc. During its embryonic period the animal is unable to take in food materials from outside in the usual way (ingestion), and special mechanisms are therefore necessary for the nutrition of the embryo. These mechanisms are of three general types:

(1) In most animals the embryo is nourished by *yolk* stored within the egg-cell before fertilization. This stored food material consists of proteins, lipins (fat, lecithin,

cholesterol) and, in some kinds of eggs, glycogen. During embryonic development these substances are in part oxidized to liberate energy, in part synthesized into more complex substances (nucleoproteins, etc.) to build the structures of the embryo. In general, the greater the amount of yolk in the egg, the more advanced is the stage of development attained by the embryo before it hatches from the egg. Some of the lower invertebrates, with relatively little yolk, emerge from the egg membrane as blastulae, others as early gastrulae, and are self-supporting throughout their subsequent development. Animals with larger amounts of yolk (*e.g.*, insects, fishes, amphibia, etc.) reach a much more advanced stage, with most of their organs fully formed, before hatching.

(2) In some animals the embryo is nourished, in part, by extracellular nutritive substances secreted by special glands of the mother before the eggs are laid. In earthworms, for instance, the cocoon within which fertilization and development occur (p. 388) contains an albuminous fluid secreted by epidermal gland cells of the mother, which serves as nourishment for the embryos; the young worms emerge from the cocoon with almost all their adult structures well developed. In reptiles and birds each egg-cell, besides containing a very large amount of yolk, is surrounded by a layer of nutritive material—the white of the egg—secreted by gland cells of the oviduct after fertilization of the egg; this is finally surrounded by a protective shell, also secreted by the oviduct, before the egg is laid. The food substances of the egg white, chiefly protein (egg albumin), are absorbed by the embryo during its development.

(3) In most mammals (and also in a few species of sharks and lizards) the embryo is nourished by food substances obtained by osmosis from the blood of the mother. In other viviparous animals (p. 389) the embryo is nourished in the usual way, by means of yolk, and has no intimate connection with the mother during its development, the egg lying free within the uterus. In the mammals (with the exception of the monotremes, a small group of oviparous mammals) the egg-cell is very small and contains almost no yolk; the embryo obtains practically all its nourishment from the

mother. In most mammals there is a special organ, the *placenta*, by which the embryo is intimately connected with the wall of the uterus. The placenta is a compound organ, formed partly by certain structures of the embryo, the *embryonic membranes*, and partly by the tissues of the maternal uterus. The embryonic membranes, the *amnion* and *allantois*, are formed by the embryos of all higher vertebrates (reptiles, birds, and mammals). The amnion originates, soon after the formation of the coelom, as a fold

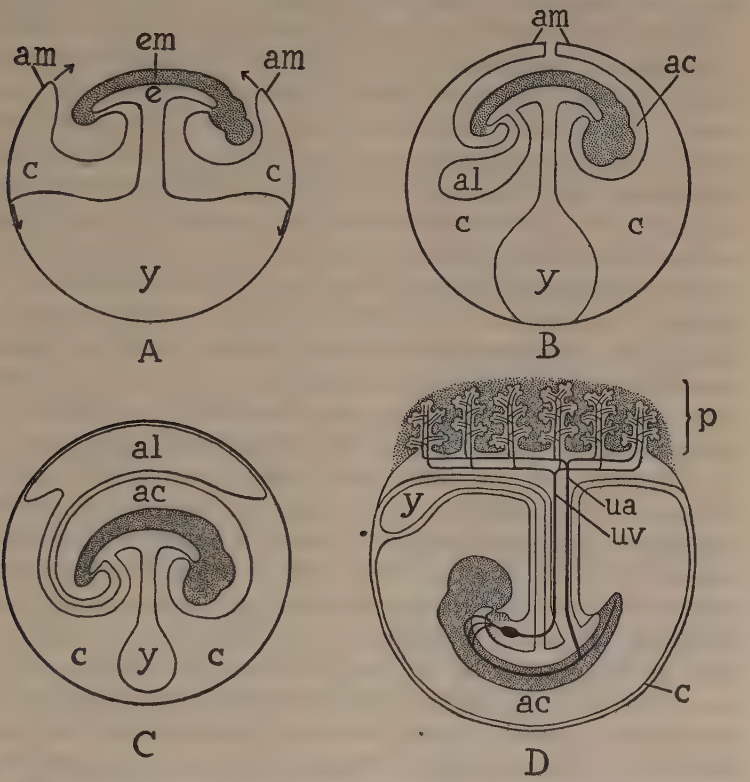


FIG. 134.—Diagrams showing development of the embryonic membranes and the placenta. *A*, amnion growing out around the embryo; *B*, amnion about to close, allantois growing out into the extra-embryonic coelom; *C*, amnion complete, allantois fusing with outer wall of the extra-embryonic coelom; *D*, placenta fully developed. *em*, embryo; *e*, enteron; *y*, yolk sac; *am*, amnion; *c*, extra-embryonic coelom; *ac*, amniotic cavity; *al*, allantois; *ua*, umbilical artery; *uv*, umbilical vein; *p*, placenta, its maternal portion shaded (maternal blood vessels not shown), embryonic portion unshaded with embryonic blood vessels indicated.

of the body wall, containing an extension of the coelom, which grows out all around the embryo and finally completely surrounds it. Into this extension of the coelom, the allantois grows out as a hollow outgrowth of the enteron, near its posterior end (the region of the cloaca), and eventually almost fills this cavity, fusing with its outer wall. The wall of the allantois develops an extensive system of blood vessels, connected with the heart by arteries and veins. In reptiles and birds, this membrane comes into close contact with the egg white and the egg shell: the blood vessels of the allantois serve for *absorption* of the egg albumin and for *respiration* of the embryo (through the porous egg shell); its cavity serves as a urinary bladder, receiving the products of *excretion* from the cloaca (the urinary bladder of the adult develops directly from the allantois). In mammals, the outer surface of the embryonic membranes grows out into numerous branching projections, called *villi*, which penetrate the tissues of the wall of the uterus. The villi are richly supplied with blood vessels of the embryo, and the uterine wall with those of the mother. There is thus established a close contact between the blood capillaries of the embryo and those of the mother; the entire structure by means of which this relation is established, including both embryonic and maternal tissues, is called the *placenta*. Here the blood of the embryo is separated from that of the mother by only a very thin layer of tissue (the walls of the blood capillaries and the villi); through this thin membrane osmotic exchanges occur between the two blood streams. In this way the embryo obtains dissolved food substances, including oxygen, from the mother, and gives off its waste products, including carbon dioxide; the placenta thus serves the embryo as an organ of *food absorption*, *respiration*, and *excretion*. It should be noted that these exchanges between the maternal and embryonic bloods take place *only by diffusion* through the intervening membrane; the blood of the embryo is formed by the embryo itself, just as in other animals (p. 401), and at no time actually mixes with the blood of the mother, only diffusible solutes being exchanged between the two. As development advances, the connection between the placenta and the rest of the embryo becomes longer and narrower, forming the *umbilical* *cord*, which is severed at birth. In some mammals, the embryonic portion of the placenta separates from the maternal portion at birth; in others (including man) the whole placenta, including some maternal tissue, is thrown off.

Parental care of eggs and young.—Many aquatic animals (invertebrates, fishes, amphibia) simply shed their eggs in the water and give them no care or attention whatever. Land animals, as a rule, at least lay their eggs in more or less protected situations or on materials suitable as food for the young. A number of animals carry the eggs, and sometimes the young, attached in some way to one of the parents; either the male or the female may do this, but usually only one sex does it in any given species. A number of crustacea carry the eggs, and the young for a short time after hatching, attached to the appendages or in a special brood-pouch of the mother. Some kinds of insects and certain species of frogs carry the eggs "glued" to the back of one sex or the other. Certain fishes (the pipefish and sea-horse) carry the eggs in a brood-pouch on the ventral surface of the male. Other fishes (*e.g.*, the sticklebacks) construct elaborate nests in which the eggs and young are guarded by the male. Many other examples might be cited of parental care of eggs and young among the invertebrates and the cold-blooded vertebrates; on the whole, however, these are exceptions rather than the general rule.

The highest developments of parental instincts are found among the social insects (ants, bees, and wasps) and the warm-blooded vertebrates (birds and mammals). The ants and the social species of bees and wasps carefully and systematically guard and feed their young right up to the adult stage; most of this work is done, not by the actual parents, but by the *workers*, which are sterile (*i.e.*, non-reproductive) females.

Among the birds, almost all species *incubate* their eggs, *i.e.*, sit on them, keeping the eggs at a temperature close to the body temperature of the adults (p. 218), which is necessary for the development of the embryos. Many birds (song-birds, pigeons, etc.) are naked, blind, and quite helpless for some time after hatching, requiring to be fed and kept warm by the parents. Other birds (chickens, ducks, ostriches, etc.) are more fully developed at the time of hatching, being covered with down or feathers and able to run about and feed themselves; but these also remain with the parents for some time for protection.

All mammals feed their young, for some time after birth, with *milk*, secreted by the *mammary glands* of the mother. The stage of development attained before birth varies widely in different kinds of mammals. In the marsupials (the lowest group of viviparous mammals, including the kangaroos, opossums, etc.), in which there is no true placenta, the young are born in a very immature state and are carried in a special pouch (the *marsupium*) on the ventral side of the mother until they are well developed. The young of placentate mammals are much further developed than those of marsupials at birth, but show wide variation in this respect; *e.g.*, mice are born naked, blind, and quite helpless, while the young of horses and cattle are born covered with hair, able to see and to stand and walk; other mammals (*e.g.*, man) are born at various stages intermediate between these extremes. The duration of parental care also varies greatly in different mammals, reaching its greatest length in man.

In general, the number of eggs produced by each kind of animal shows an inverse relation to the provisions for nutrition of the embryo and the care of eggs and young; *e.g.*, the lower invertebrates, with little yolk in their eggs and no parental care, produce enormous numbers of eggs, while in higher animals the number of eggs decreases progressively with the development of better embryonic nutrition and parental care. In the former case, only a very small proportion of the total eggs ever survive the vicissitudes of development and growth to produce adult animals; in the latter case each individual egg and young animal has a much better chance of survival. On the whole, under natural conditions, each species of animals just about maintains its numbers constant from generation to generation—either by the wasteful method of producing a great excess of eggs or by the more economical methods of enhancing the chance of each individual to survive to maturity.

Metamorphosis.—In some animals the young, at hatching or birth, resemble the adults of their species fairly closely in external form and most of their internal structures; their post-embryonic development consists chiefly of increase in size. This is true of many of the more familiar animals (*e.g.*, the higher vertebrates) but is by no means the general rule. In many groups of animals the young, for some time after hatching, differ markedly from the adults—so much that they would never be recognized as belonging to the same species or even the same group of animals. These differences involve not only the external form, but often many of the internal organs also. The young may lack entirely some of the organs of the adults, and may possess organs not present in the latter; they may differ radically in their behavior, methods of food-getting and respiration, the kind of places they inhabit, etc. In such cases the young animal is called a *larva*, and its transformation into the adult form is called *metamorphosis*.

The most striking examples of metamorphosis among vertebrates are the amphibia. In most of this group, the larvae are strictly aquatic fish-like animals breathing by means of gills, while the adults are terrestrial or semi-terrestrial animals breathing by means of lungs. The external changes during metamorphosis are especially striking in the tailless amphibia (frogs and toads), whose larvae (tadpoles) have tails but no legs. During metamorphosis the tail gradually disappears; its tissues are actually consumed by phagocytic cells (p. 272) and their materials utilized as food substances for the growth of other organs. At the same time the legs are growing rapidly, and the whole body form changes markedly. Concurrently with these external changes, very important changes occur in some of the internal organs. The lungs develop at the same time that the gills are degenerating, thus converting the animal from a "water-breathing" to an "air-breathing" form. Important changes occur also in the circulatory and digestive systems.

Among the invertebrates, metamorphosis is the rule rather than the exception; in most cases the young hatch as larvae which differ markedly from the adult form. Among the most extreme cases of metamorphosis are those of many insects (*e.g.*, butterflies and moths, beetles, bees, flies, etc.), whose larvae are worm-like animals, called caterpillars.

grubs, or maggots, which bear no external resemblance to the adult insects. After a period of active feeding and growth, these larvae transform into non-motile forms called *pupae.* In some cases (*e.g.*, moths) the larvae spin silken cocoons about themselves before pupation; in others (*e.g.*, flies), the pupa remains within the dead, dried-up larval skin. During this quiescent period, many of the larval tissues and organs disintegrate entirely or are consumed by phagocytic cells, so that the interior of the pupa consists largely of structureless liquid material, which is utilized as food for the development of the adult structures. Most of the external parts and also many of the internal organs of the adult insect develop from small groups of undifferentiated cells of the larva. At the end of the pupal stage, the adult insect emerges, fully developed, from the cocoon or the pupal skin; there is no further development or growth thereafter. While these phenomena are especially striking in insects, a number of other invertebrate groups exhibit almost as extreme metamorphoses, the whole of the adult structures being developed from a relatively small portion of the larval tissues.

Development of the germ cells.—All the cells which make up the body of a multicellular animal—many billions of them in the higher animals—are derived from the unicellular zygote (fertilized egg-cell) by an unbroken series of cell divisions. Of these cells the great majority are *somatic cells* (p. 367), which take no part in reproduction of the organism and are therefore destined to die when the individual organism dies. A relatively small proportion of the cells of the animal are *germ cells*, which may, under proper conditions, produce new individuals, including their germ cells, and so on forever: the germ cells are *potentially immortal.* In the term "germ cells" we include not only the gametes but *all those cells in the line of descent of the gametes*, from the unicellular zygote through successive cell generations to the mature gametes. By this definition, all cells which give rise to both somatic and germ cells, or to germ cells only, are germ cells; somatic cells produce only somatic cells. In some animals, the germ cells are distinguishable from somatic cells very early in embryonic development—even as early as the cleavage divisions—by visible peculi-

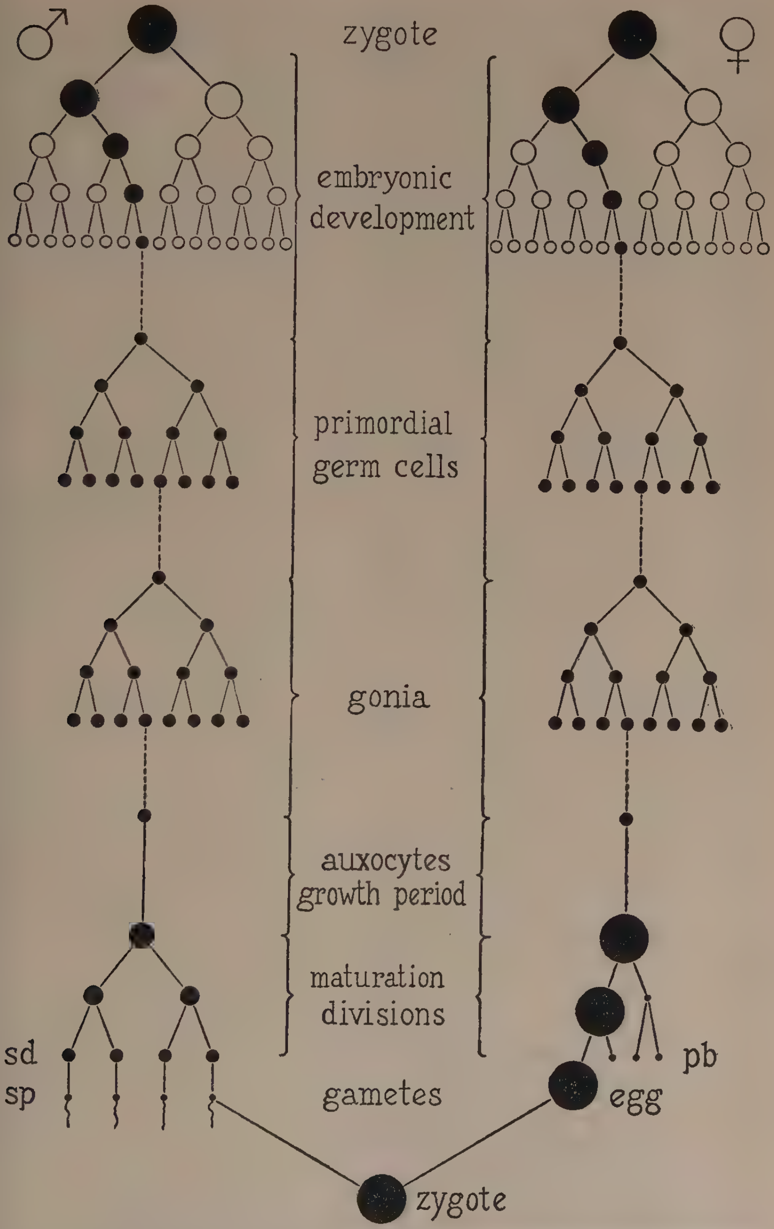

♂
zygote
♀
embryonic development
primordial germ cells
gonia
auxocytes growth period
maturation divisions
sd
sp
pb
gametes
egg
zygote

FIG. 135.—Diagram of the history of the germ cells in multicellular animals; germ cells black, somatic cells white. The number of cell divisions is, of course, actually much greater than shown here (except in the maturation period). *pb*, polar bodies; *sd*, spermatids; *sp*, sperms. (Adapted from Wilson.)

arities of the nucleus or the cytoplasm or both. In the roundworm Ascaris, the chromosomes of *one* of the first two cells, produced by the first cleavage division of the zygote, undergo a peculiar process of fragmentation; all the cells derived from this one, which can be recognized by their fragmented chromosomes, are exclusively somatic cells. In the other cell of the two-cell stage, the chromosomes divide regularly, but the process of fragmentation occurs again in *one* of its daughter cells, so that there are now three cells with fragmented, and one with normal, chromosomes. This process recurs at each cell division until the 16-cell stage, when there are 15 cells with fragmented, and one with normal, chromosomes; the former produce only somatic cells, the latter, by further normal divisions, produces the germ cells. In some other animals also—some worms, crustacea, and insects—the germ cells are identifiable by nuclear or cytoplasmic peculiarities in the early cleavage divisions. This condition, however, is exceptional; in most animals the germ cells can not be visibly distinguished from somatic cells until much later in development. In some cases the germ cells, when first distinguishable, are found in parts of the body quite distant from their final location in the gonads, to which they migrate by amoeboid movement. In many vertebrates they have been found, at an early embryonic stage, in the endoderm, from which they migrate later, through the mesentery, to the coelomic epithelium in the region where the gonads subsequently appear (Fig. 62). In most animals the germ cells are first distinguishable in the coelomic epithelium in the region of the gonads, at or shortly before the time when these organs begin to be formed.

The germ cells are at first simple undifferentiated cells, not visibly different from any other embryonic cells, and apparently just alike in the two sexes. These *primordial germ cells* multiply rapidly, by mitotic divisions, forming a large number of cells, called *gonia* (*spermatogonia* in the male, *oogonia* in the female), which—together with a certain amount of somatic tissue, serving for their nutrition and mechanical support—make up the gonads. After a time the germ cells cease to divide, and enter a prolonged *growth period:* at this stage they are called *auxocytes* (*spermatocytes* in the male, *oocytes* in the female). The growth period is much longer in the oocytes, in which during this period the *yolk* is formed and the relatively enormous size characteristic of the egg-cell is attained. At the end of the growth period each auxocyte undergoes *two* final cell divisions, producing the *gametes*. These last two divisions are called the *maturation divisions:* one of them (either the first or the second) is the *reduction division* (p. 374), the other is essentially an ordinary mitotic division. All the germ cells of an individual animal do not pass through these stages simultaneously; in a mature gonad we usually find germ cells in all stages from gonia to mature gametes.

In the nuclei of the auxocytes, during the growth period, occurs a complex series of chromosomal phenomena, leading up to the reduction division. It will be recalled (p. 391) that every cell of the animal body, except the gametes, has the *diploid* number of chromosomes, consisting of one haploid set derived originally from each parent. In all the somatic cells and also in the germ cells through the gonial stage, all these chromosomes remain perfectly separate from each other, each maintaining its own individuality, growing during each intermitotic period and dividing at each mitosis. In the auxocytes, at the beginning of the growth period, the chromosomes *join in pairs;* this process is called *synapsis*. Each pair of chromosomes, thus formed, is called a *bivalent;* the single chromosomes are called *univalents; i.e.*, each bivalent is composed of two univalents or ordinary chromosomes. The association in pairs is not at random; each bivalent consists of one chromosome derived originally from each parent, *i.e.*, one from each of the two haploid sets which combined to form the zygote nucleus at fertilization (p. 391). Moreover, each particular chromosome of one set always pairs with one particular chromosome of the other set, the two chromosomes of the pair being (in general) of exactly the same size and shape. The two chromosomes which pair at synapsis are called *homologous chromosomes;* these can, in many cases, be identified as such in every mitosis by their similarity in size and shape. Just before synapsis the chromosomes are in the form of long thin threads (as in the early prophases of mitosis); at synapsis the two homologous chromosomes of each pair come to lie close together, side by side, and, in many cases, *appear* to fuse completely, forming a single thicker thread. Since the total number of chromosomes (univalents) is $2n$ (the diploid number), the number of "thick threads" (bivalents) is n (the haploid number); there has thus been an *apparent* reduction of the chromosome number from $2n$ to n. This apparent reduction in number is not real, however, for sooner or later each "thick thread" divides again, by a longitudinal split, into two univalents, which continue to lie close together side by side. These two univalents may not be identical, individually, with the two which joined

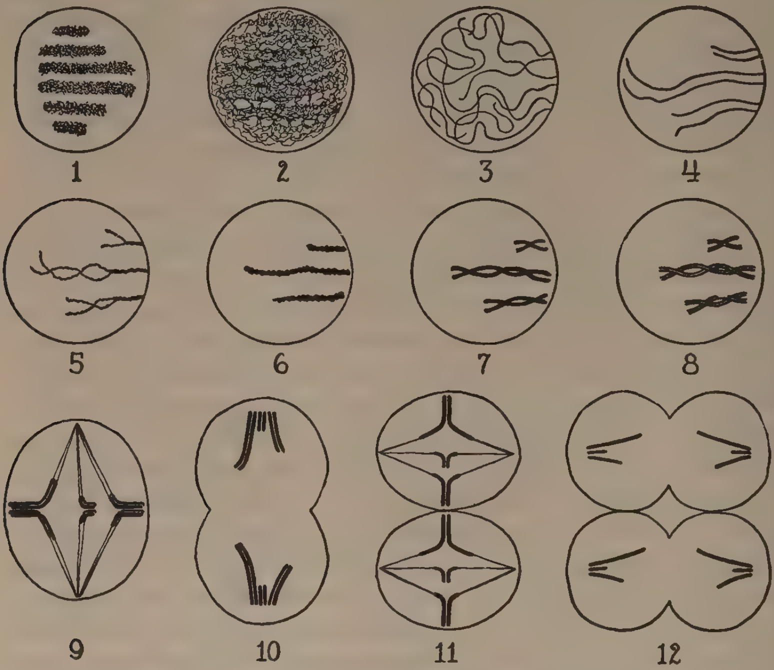


FIG. 136.—Diagram of synapsis and reduction. In this diagram the haploid number of chromosomes is three, and these are distinguished from each other by differences in length. *1*, telophase of last gonial division, showing the diploid number of chromosomes; *2*, intermitotic ("resting") stage of early auxocyte; *3*, *4*, thin-thread stages, showing diploid number of univalent chromosomes, beginning to pair; *5*, synapsis of homologous chromosomes; *6*, thick-thread stage, showing haploid number of bivalents; *7*, bivalents splitting longitudinally; *8*, second longitudinal split, converting each bivalent into a tetrad; *9*, *10*, first maturation division, dividing each tetrad into two dyads; *11*, *12*, second maturation division, resulting in four haploid nuclei.

originally to form the bivalent, for in some cases there is an exchange of material between the two homologous chromosomes during synapsis, so that each of the post-synaptic univalents contains chromatin from both of the original members of the pair. This process, called *crossing-over*, always involves an exactly equal interchange between the two chromosomes, so that each of the post-synaptic univalents is *quantitatively equivalent* to one of the original presynaptic univalents. At the same time, or a little later, each univalent also splits longitudinally into two daughter chromosomes, as in an ordinary mitotic division (p. 352); thus each bivalent is converted into a *tetrad*, or group of four threads. The condition now is similar to the late prophases of ordinary mitosis, when each of the *2n* chromosomes is divided into two daughter chromosomes, except that here they are grouped in tetrads. This grouping persists until the maturation divisions, which resemble ordinary mitotic divisions in most respects except that the two divisions occur in rapid succession without any further splitting of the chromosomes. The two maturation divisions result in the formation of four cells from each auxocyte; the nucleus of each of these four cells receives one daughter chromosome from each tetrad, and therefore contains *n* chromosomes (one haploid set). The gametes develop directly from these cells, without further divisions; thus each gamete nucleus contains *one complete haploid set of chromosomes*, *i.e.*, one representative of each pair of homologous chromosomes. The *numerical* relations of the chromosomes during these stages may be summarized thus: the original auxocyte nucleus (like that of a somatic or a gonial cell) contains *2n* chromosomes (univalents); at synapsis these pair to form *n* bivalents; the bivalents split twice, giving *n* tetrads; each gamete nucleus receives *1* component of each tetrad, and therefore contains *n* chromosomes. One result, therefore, of the maturation divisions is the reduction of the chromosome *number* from *2n* in the original auxocyte nucleus to *n* in the gamete nucleus. Which of the two maturation divisions is the reduction division? That depends entirely on which way the tetrads happen to divide in each of the two divisions: if the homologous chromosomes separate from each other in the first division, and the daughter halves of each univalent separate in the second division, then the first division is the reduction division and the second is an ordinary, or *equational*, division; but if the daughter halves of each univalent separate in the first division, as in an ordinary mitosis, then the second division becomes the reduction division. In most cases, it is impossible to tell which of these actually occurs, because the four components of a tetrad, usually, all *look* exactly alike. In particular cases where it is possible to answer this question, the reduction division is sometimes the first maturation division, sometimes the second, or each division may be reductional for some tetrads and equational for others. The end result is the same in either case: each gamete nucleus contains n chromosomes, including one representative of each pair of homologous chromosomes. In addition to the reduction in chromosome number, the processes of synapsis and maturation have other, less obvious but no less important, results: the extensive reassortment of individual chromosomes and of their component genes among the haploid sets, so that very few of the gametes produced by one individual are identical in their qualitative composition. These results, which are of fundamental importance in the phenomena of heredity, will be discussed later (Chapter XXII).

The processes we have been describing, involving the chromosomes, are essentially similar in the maturation of sperm and egg cells. The cytoplasmic phenomena accompanying them are, however, very different in the two sexes. We have already mentioned the fact that the oocytes grow for a much longer time and attain a much larger size than the spermatocytes, before maturation. At the maturation divisions, each spermatocyte divides into four equal cells, called *spermatids*. Each spermatid is converted into a spermatozoon, or sperm-cell, by the elimination of most of its cytoplasm and of its nuclear sap (the non-chromatinic material of the nucleus), retaining only its chromatin and certain relatively small cytoplasmic structures (p. 387). These processes are completed within the testis (spermary) from which the sperm-cells are discharged in their mature and fully developed form. The oocyte divides in a very different way. The divisions of the chromosomes are just as in the spermatocyte, but the cytoplasm divides very unequally, practically all of it, at each maturation division, remaining in one cell. The final products of the two maturation divisions are therefore *one* large egg-cell, almost as large as the original oocyte and containing practically all its cytoplasm and yolk, and *three* very small cells, called *polar bodies*, consisting practically of nuclei only. The polar bodies (normally) play no further rôle and soon degenerate. Thus, while each spermatocyte produces four functional sperm-cells, each oocyte produces only one functional egg-cell. The maturation divisions of the oocyte are usually not completed until after it has been discharged from the ovary, and in many animals not until after it has been entered by the sperm; in such animals the maturation divisions stop at a certain stage (which differs in different species) and do not continue until the egg has been activated by the entrance of the sperm, or artificially (p. 391). In every case, however, the maturation divisions are completed before the union of the sperm and egg nuclei, so that these two nuclei are always equivalent; *i.e.*, each contains the haploid number of chromosomes. The union of the sperm and egg nuclei restores the diploid number, as previously explained (p. 391), and initiates another cycle of development, growth, and reproduction.

Asexual reproduction.—As previously mentioned, sexual reproduction is practically universal among multicellular animals, and most of them have no other method of reproduction. A number of animals (chiefly invertebrates), however, reproduce also by asexual methods. The term asexual reproduction includes all methods of producing new individuals not involving fertilization. The methods of asexual reproduction found among metazoa include: *parthenogenesis*, the development of new individuals from unfertilized egg-cells; *fission* and *budding*, the production of new individuals from multicellular portions of the parent animal.

Parthenogenesis.—In a number of animals eggs may develop naturally without fertilization: this is called *parthenogenesis*. In some species, this may be merely an occasional and perhaps accidental event: their eggs are unusually "sensitive" and may be activated by some relatively slight change of external conditions such as may occur in the natural environment of the organism. But in several groups of animals—including especially the rotifers, some of the smaller crustacea ("water-fleas," etc.), and various insects (aphids, gall-flies, ants, wasps, bees, etc.)—parthenogenesis is a normal and regular mode of reproduction. Almost all of these animals also reproduce sexually; the relations between sexual reproduction and parthenogenesis vary widely in the different groups.

Two main types of normal parthenogenesis may be distinguished: *haploid parthenogenesis*, in which the egg develops with the haploid number of chromosomes, and *diploid parthenogenesis*, in which the parthenogenetically developing egg has the diploid number of chromosomes like the sexually produced zygote. The first type occurs in all ants, wasps, and bees, and in a few other animals. In these animals all the oocytes undergo the two maturation divisions in the usual way, and the eggs therefore have the haploid chromosome number. These eggs may either be fertilized or may develop parthenogenetically: the fertilized eggs, with the diploid chromosome number, produce *only females*, the unfertilized eggs, with the haploid chromosome number, produce *only males*. All the males therefore have the haploid number of chromosomes in every cell and produce sperm-cells *without a reduction division;* they are comparable, in this respect, to those algae (Spirogyra, etc.) which have the haploid number in all their ordinary cells and produce gametes by ordinary mitoses (p. 375). The females, however, are diploid, like other animals, and produce egg-cells by the usual process of maturation.

Diploid parthenogenesis is more frequent, occurring in various insects, crustacea, worms, and other animals. In these animals, the parthenogenetic eggs have only one maturation division, producing a single polar body, and this division is equational (*i.e.*, an ordinary mitosis); there is therefore no reduction of the chromosome number, and the eggs are diploid. These eggs are incapable of fertilization, and produce, parthenogenetically, either males or females. In many of these animals the parthenogenetic (diploid) and the ordinary (haploid) eggs are produced by different generations of females, which often differ markedly in external appearance and behavior. The relations between the parthenogenetic and the sexual generations, which vary somewhat in different cases, may be exemplified by the aphids ("plant lice"). During the summer these insects have a series of generations consisting of females only, which are strictly parthenogenetic, all the eggs being diploid. Toward the end of the summer some of these parthenogenetic eggs produce *males* and others produce *sexual females*. The oocytes of the sexual females undergo two maturation divisions of the usual type, and their eggs are therefore haploid. These eggs are incapable of developing without fertilization; when fertilized, the zygotes produce (in the following spring) *parthenogenetic females*, initiating another series of asexual generations. If the aphids are raised in a greenhouse, under uniform environmental conditions the year round, the sexual generation may not ap-

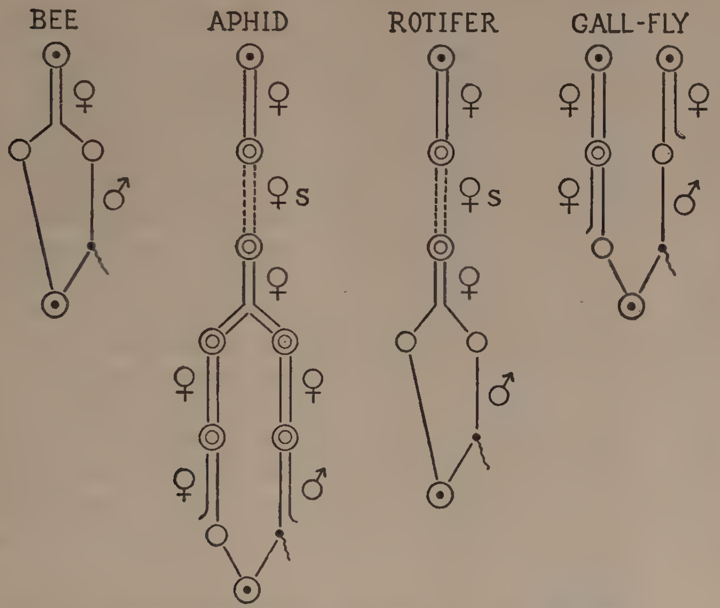


FIG. 137.—Diagrams of several types of life-cycles involving parthenogenesis. Single lines represent the haploid, double lines the diploid, condition; simple circles represent haploid eggs, double circles diploid eggs, circles enclosing a black dot zygotes. In the aphid and the rotifer the number of successive generations of parthenogenetic females is indefinite. (Adapted from Wilson.)

pear at all, reproduction continuing solely by parthenogenesis through a series of years. In a few animals reproducing by diploid parthenogenesis—some roundworms and some species of aphids, scale-insects, gall-flies, walking-sticks, and other insects—sexual reproduction seems to have been lost completely, males being entirely unknown. These are probably the only metazoan animals which have no sexual reproduction.

Some animals—rotifers and some gall-flies—have both diploid and haploid parthenogenesis. In the rotifers there is a series of asexual generations of females reproducing by diploid parthenogenesis only, just as in the aphids. Under certain environmental conditions, this parthenogenetic reproduction may go on for years; but under different conditions (such as a change of diet) some of the eggs develop into sexual females, whose oocytes undergo two maturation divisions, producing haploid eggs. These haploid eggs behave like those of the bee: if unfertilized they produce males, by haploid parthenogenesis; if fertilized they produce females, which initiate another series of asexual generations. In some of the gall-flies there is a regular alternation of asexual and sexual generations, apparently independent of environmental conditions: the fertilized eggs produce only parthenogenetic females, which in turn produce either males, by haploid parthenogenesis, or sexual females, by diploid parthenogenesis.

In certain flies, the larvae reproduce parthenogenetically: several generations of larvae may be produced in this way; then the larvae of the last generation pupate and develop into adult sexual males and females. Reproduction (whether asexual or sexual) by larvae is called *pedogenesis*.

Artificial activation of eggs by chemical or physical agents (p. 391) is commonly called "artificial parthenogenesis." This process resembles natural parthenogenesis in that the eggs develop without true fertilization; on the other hand, it resembles fertilization in that the development of the egg is initiated by an external stimulus, whereas in normal parthenogenesis no external stimulus seems to be necessary. A process comparable to artificial activation which may sometimes occur under natural conditions is the activation of the egg by sperm of a different, not closely related, kind of animal (p. 392). In this case the foreign sperm activates the egg, initiating its development, but the sperm nucleus does not unite with the egg nucleus and takes no part in the development. All these processes—natural parthenogenesis, artificial and "accidental" activation—differ from fertilization in one important respect: the animal so produced derives all its chromosomes (whether haploid or diploid in number) from those of the egg-cell and therefore *from one parent only*, while in sexual reproduction the chromosomes of the zygote are always derived from two gametes (egg and sperm cells) and usually *from two parents.*

Fission and budding.—The division of an organism into two or more equal, or nearly equal, fragments, each of which becomes a new individual, is called *fission;* the formation of a new individual from a relatively small portion of the parent organism, which maintains its own size and form practically unchanged, is called *budding:* the distinction between these two methods of reproduction is not very sharp. It will be recalled that these terms are applied to the equal or unequal division of unicellular organisms (pp. 363, 364). A number of multicellular animals also reproduce by fission or budding; in these cases, the fragments or buds are multicellular portions of the parent animal.

Complete fission of the body into two or more parts, each forming a separate individual, occurs in some species of coelenterates, flatworms, annelids, and echinoderms, in either the larval or the adult stages. In some other animals fission may occur in an early embryonic stage, resulting in the production of two or more embryos from one egg: this is called *polyembryony.* In some of the parasitic Hymenoptera (insects related to the wasps and bees), hundreds of individuals may thus be produced from a single egg (either fertilized or parthenogenetic). In at least one species of mammals, the Nine-banded Armadillo, polyembryony is normal, four young being regularly produced from each egg. Polyembryony also occurs occasionally in other animals, including man, where it results in the production of twins of the type called *identical twins*, who bear an extraordinary resemblance to each other in every respect; this close resemblance is due to the fact that both twins contain exactly the same set of chromosomes and of genes (having been produced from the same zygote by ordinary mitotic divisions) and are therefore identical in every respect except for differences which may be caused by environmental factors. Incomplete fission of the embryo may produce "Siamese twins," double-headed monsters, etc.

Reproduction by budding occurs in some flatworms and annelids, and in most coelenterates, sponges, Bryozoa, and tunicates. In some of these animals, the buds separate from the parent, becoming completely separate individuals. In Hydra, which reproduces asexually in this way, the bud starts as an outgrowth of the body wall at one point; it elongates and develops a mouth and tentacles at the free end; then the bud separates from the parent animal, becoming a separate individual. In many other coelenterates, however, the buds remain permanently attached to the parent, forming complex *colonies*. There is often a con-

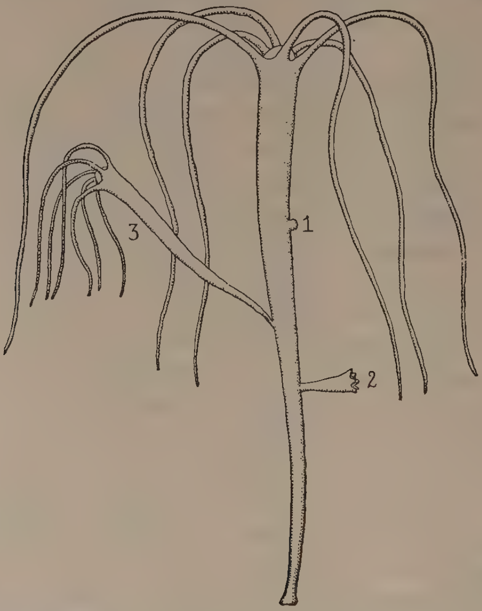


FIG. 138.—Hydra budding. *1, 2, 3,* buds in successive stages of development.

siderable degree of differentiation among the individuals, or *zooids*, composing such a colony. In some cases, a majority of the zooids are entirely asexual, gonads being developed only by certain specialized members of the colony. In other cases all the zooids composing the colony are asexual, the gonads being developed in free-swimming individuals, called *medusae*, which are produced by budding from some of the asexual zooids. A few other groups of metazoa—sponges, Bryozoa, and tunicates—also form colonies of connected individuals by budding. Some species of sponges and of Bryozoa also reproduce asexually by means of *internal buds*, which are small groups of cells, produced within the body of the animal and enclosed by protective envelopes; these are able to survive unfavorable conditions and, on the return of favorable conditions, develop into new individuals.

Regeneration.—Closely related to reproduction by fission and budding is the process of *regeneration*—the restoration of parts of an organism which have been accidentally lost or injured. All organisms possess the power of regeneration to a greater or less extent, but it is, in general, much more limited in the higher animals than in lower animals and in plants. In many of the lower metazoa—sponges, coelenterates, flatworms, annelids, echinoderms, etc.—a small fragment of the body may regenerate a whole animal. Since several or many individuals may thus be produced from one, this is actually a mode of asexual reproduction, though not a normal one. Some of these animals break into fragments so readily that it is difficult to draw a sharp line between regeneration as a result of accidental injury and normal reproduction by fission.

In the higher animals—*e.g.*, molluscs, arthropods, and vertebrates—the power of regeneration is more limited. Many of these animals can regenerate a small portion of the body, such as a limb, which has been lost or injured—but the limb can not regenerate a whole animal; and if the whole body be divided into two or more parts all the parts die. Among the vertebrates, fishes can regenerate fins and tails; salamanders can regenerate tails, legs, and jaws; adult frogs can not regenerate legs, but the tadpoles can. None of the higher vertebrates can regenerate limbs; lizards can regenerate tails, but other reptiles can not. In mammals, the regeneration of external parts is limited to the growth of skin and connective tissue over wounds, but some of the internal organs—especially the liver and some other glands—have considerable power of regeneration.

CHAPTER XXI

REPRODUCTION OF MULTICELLULAR PLANTS

Most multicellular plants reproduce sexually. In addition, practically all of them also reproduce asexually by means of unicellular *spores*. Many plants also have other asexual methods of reproduction, which will be discussed later (p. 449).

In all plants above the thallophytes there is a regular *alternation* of sexual and asexual generations. The sexual, gamete-producing plant, all of whose nuclei normally contain the *haploid* chromosome number, is called the *gametophyte;* the asexual, spore-producing, plant, whose nuclei are normally *diploid*, is called the *sporophyte* (p. 376). The relative development of these two generations, and their nutritive relations to each other, differ greatly among the different groups of plants. The relations in the four major plant groups (omitting the schizophytes, which have no sexual reproduction) may be indicated briefly as follows:

Thallophyta (algae and fungi).—In most species, there is no diploid generation, reduction occurring during the first nuclear divisions of the zygote. Many of these plants also reproduce asexually by spores, but spores and gametes are usually produced by the same individual plant and there is no alternation of sexual and asexual generations; exceptions will be noted below (p. 424).

Bryophyta (liverworts and mosses).—There is a regular alternation of sexual and asexual generations, but the sporophyte always remains permanently attached to the gametophyte and dependent on it for nutrition (p. 427).

Pteridophyta (ferns and related plants).—Both generations are usually independent (exceptions will be noted below, p. 430), but the sporophyte is always the larger, more complex, and longer-lived.

Spermatophyta (seed-plants).—The gametophyte consists of only a few cells, is completely dependent on the sporophyte for nutrition, and the female gametophyte remains permanently attached to and enclosed by the sporophyte (p. 434).

The accompanying diagram (Fig. 139) indicates roughly the relative durations of the two generations in each of these groups. In the following pages we shall describe the life cycles of some typical representatives of each group.

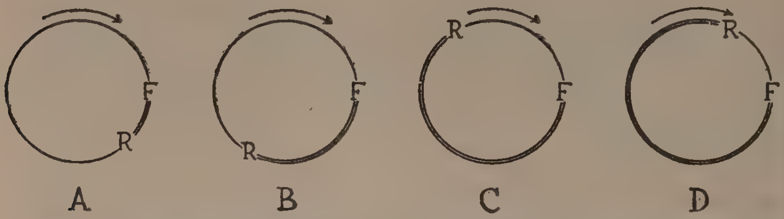


FIG. 139.—Diagrams illustrating the relations of the haploid and diploid stages in the four major plant groups: *A*, most thallophytes; *B*, bryophytes; *C*, pteridophytes; *D*, spermatophytes. Single lines represent the haploid, double lines the diploid, condition; *F*, fertilization; *R*, reduction.

Thallophytes.—This group includes plants of various degrees of complexity, from unicellular forms (Pleurococcus, yeast, etc.) through simple colonial forms (Spirogyra, Gonium, etc.), to fairly complex multicellular plants (Nitella, seaweeds, mushrooms, etc.). The reproductive methods of some of the simpler thallophytes have been discussed previously (Chapter XIX). The higher algae and fungi show a great variety of reproductive methods, both sexual and asexual, differing in the forms of their gametes and spores, the structure of the organs in which these are produced, the succession of different reproductive methods in their life cycles, etc. This group of plants, in fact, probably exhibits as great a variety of reproductive phenomena as all other organisms put together.

The relations of the haploid and diploid phases in the life cycles of some of these plants have already been briefly mentioned (p. 376). As there indicated, three very different relations are found in different species of thallophytes: (1) usually the reduction division immediately follows fertilization, a relation found only in this group of plants and in a few protozoa; (2) in some algae there is an alternation of haploid and diploid generations, as in higher plants;

(3) in a few algae reduction immediately precedes fertilization, as in animals. These three main types include endless variations in details, and are more or less connected by intermediate forms.

(1) In most thallophytes, the first two divisions of the zygote nucleus after fertilization closely resemble the two maturation divisions in the germ cells of animals (p. 411), involving synapsis and reduction. In some algae (*e.g.*, Spirogyra) three of the four nuclei thus formed degenerate—as in the maturation of the animal egg—and the single resulting cell then develops directly, by ordinary mitotic divisions, into a new plant (p. 375). More usually, all four

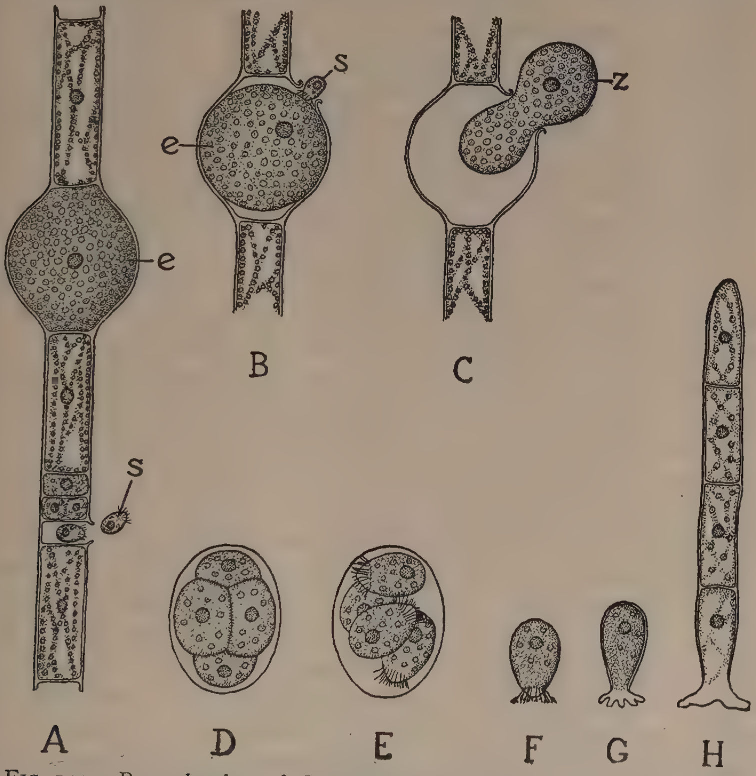


FIG. 140.—Reproduction of Oedogonium, a filamentous green alga. *A*, portion of a mature filament, showing development of sperm-cells (*s*) and egg-cell (*e*); *B*, fertilization; *C*, liberation of the zygote (*z*); *D*, *E*, division of the zygote into four spores; *F–H*, development of one of these spores into a new filament.

of these nuclei are functional and the zygote divides into four cells. In some forms (*e.g.*, Oedogonium), each of these four cells forms a *spore;* the four spores separate and each one develops into a new plant. In other forms these four cells divide further, by ordinary mitoses, and form a larger number of spores, each of which develops into a new plant. This type of reproduction, which is found in many algae and almost all fungi, resembles that of higher plants in one significant respect: the maturation divisions—*i.e.*, the divisions during which reduction is effected—produce *spores*, which develop *asexually* into haploid plants. These plants may reproduce asexually, by spores or other methods, for some time, but eventually they produce gametes (by ordinary mitotic divisions, as the nuclei are already haploid), which unite to form the diploid zygote.

(2) In some species of red algae and of brown algae, the maturation divisions and spore production are postponed for many cell-generations after fertilization; *i.e.*, the zygote develops directly, by ordinary mitotic divisions, into a plant with diploid nuclei, the sporophyte. In this plant, when it is mature, the spores are produced from cells called *sporocytes* (corresponding to the auxocytes of animals, p. 410); each sporocyte undergoes synapsis and two maturation divisions, producing four spores, which are haploid. The spores develop asexually, as in the preceding type, into haploid plants (gametophytes), which eventually produce gametes. Thus these plants have a regular alternation of a haploid, sexual, gamete-producing generation and a diploid, asexual, spore-producing generation. In most of these algae the gametophyte and the sporophyte of the same species are similar in general structure and appearance. But in some species the two generations are very different, so that they would never be recognized as belonging to the same species except by a study of the life cycle; this is also the case, as we shall see, in all the higher plants.

(3) In a few of the brown algae (*e.g.*, the common brown seaweed Fucus), all the ordinary cells of the plant are diploid and the maturation divisions produce gametes—as in animals—instead of spores. The gametes unite to form a zygote which develops directly into a diploid plant again. In these algae, therefore, there is no haploid generation;

this type of life cycle, which is the usual one in animals, is quite unusual in plants.

Bryophytes.—The most familiar representatives of this group are the mosses. The life history of any one of the common mosses will serve to illustrate the methods of reproduction in this group of plants. The familiar leafy-stemmed moss plant, whose structure and nutrition have been described previously (p. 160), is a gametophyte, *i.e.*, a haploid, gamete-producing plant. The reproductive organs are borne at the tip of the stem, surrounded by a whorl of leaves, when the plant is mature. Most mosses are dioecious, the male and female plants being distinguishable by the form of the leaves surrounding the reproductive organs. The female reproductive organs are flask-shaped structures, called *archegonia*, borne in a group at the tip of the female plant. Each archegonium contains, when mature, a single large spherical egg-cell. The male reproductive organs are club-shaped structures, called *antheridia*, borne in a group at the tip of the male plant. Each antheridium produces a large number of small flagellate sperm-cells. Each sperm-cell has two flagella at its anterior tip, by which it swims; the bulk of the sperm-cell consists of chromatin, representing a very condensed nucleus, just as in the animal sperm. As all the cells of this plant are haploid, the gametes are produced by ordinary mitotic divisions, *i.e.*, without reduction or any other peculiarity of chromosome behavior.

When the antheridia are ripe, they burst open, liberating the sperms. These swim about in the films of water, from rain or dew, on and about the plants, until they reach the archegonium of a female plant; this is one reason why mosses can flourish only in moist places. There is evidence that the archegonium secretes substances which "attract" the sperms, *i.e.*, cause them to swim toward and into the neck of the archegonium; this is a case of positive chemotropism (p. 336). One or more sperms enter the archegonium, where a single one of them fertilizes the egg-cell. The process of fertilization is, in all essential respects, similar to that of the animal egg (p. 389). The zygote thus formed has the diploid number of chromosomes, made up of one haploid set from each gamete.

Immediately or shortly after fertilization the zygote begins its development, within the archegonium of the

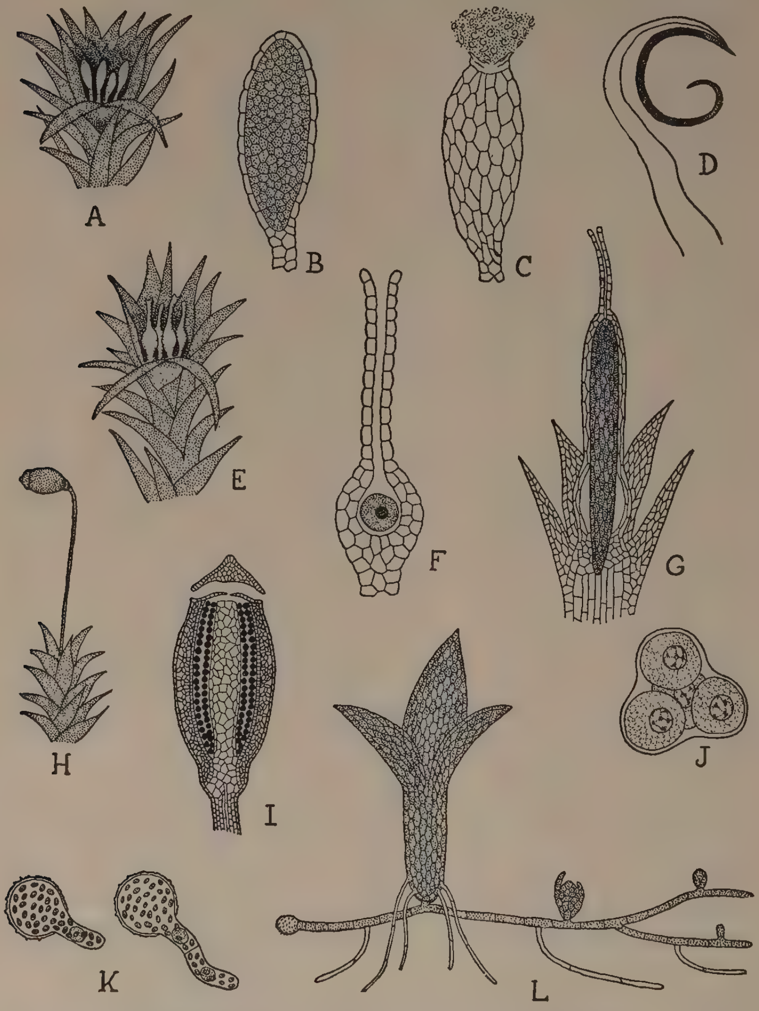


FIG. 141.—Reproduction of a moss. *A*, tip of male gametophyte, showing antheridia; *B*, an antheridium (vertical section); *C*, antheridium discharging sperms; *D*, a sperm; *E*, tip of female gametophyte, showing archegonia; *F*, a mature archegonium, showing the egg-cell (vertical section); *G*, embryo sporophyte developing within the archegonium and pushing its foot down into the tissues of the gametophyte (vertical section); *H*, mature sporophyte, attached to the tip of the female gametophyte; *I*, spore capsule (vertical section), showing spores (black), lid which falls off when the capsule is ripe, and teeth which open to liberate the spores; *J*, division of a sporocyte into four spores; *K*, germination of spores; *L*, protonema with buds developing into leafy stems.

mother plant. By a series of mitotic divisions, an elongate mass of cells is formed. The lower end, called the *foot*, pushes down into the stem of the mother plant, serving for attachment and nutrition of the embryo. The other end of the embryo grows upward into a long slender *stalk*, at the upper end of which a cylindrical *spore capsule* is formed. As it grows, it bursts the archegonium, the upper end of which adheres to the spore capsule for some time as a small conical cap. This whole structure—foot, stalk, and capsule—constitutes the sporophyte, *i.e.*, the diploid, spore-producing generation of the moss. This plant remains permanently attached, by its foot, to the mother gametophyte. The outer cells of the stalk and capsule contain some chlorophyl, and are therefore capable of photosynthesis, but the sporophyte derives most of its nutrition from the gametophyte by absorption through the foot.

Within the capsule is produced a large number of *sporocytes*. In the sporocytes occur the processes of synapsis and reduction, essentially as in the auxocytes of animals (p. 411). Each sporocyte undergoes two maturation divisions, producing four spores, each with the haploid number of chromosomes. When the spores are ripe, the capsule opens at its free end, and the spores are scattered through the air.

Each spore which alights in a suitable place develops, under favorable conditions of temperature and moisture, into a form of plant called a *protonema*. This is a branching filament of cylindrical green cells, closely resembling some of the filamentous green algae. From the protonema the erect leafy stems are produced by a process of budding. Each bud originates as a single cell derived from one of the protonemal cells by mitotic division. By continued growth and cell divisions, this bud produces the various tissues of the stem and leaves (p. 161). Several or many stems may arise from a single protonema; eventually the protonema dies off and each of these stems becomes a separate plant. These plants, when mature, develop reproductive organs and gametes, as previously described. The protonema and leafy stems, together, constitute the gametophyte generation of the moss.

The characteristic features of the life cycle of bryophytes are the regular alternation of a haploid sexual generation and a diploid asexual generation, with the former much better developed, the sporophyte being permanently attached to and dependent on the gametophyte.

Pteridophytes.—The most familiar representatives of this group are the ferns. In these plants the relative development of the two generations is very different than in the mosses. The large fern plant, consisting of roots, stems, and leaves, is a sporophyte, *i.e.*, a diploid, asexual plant. The spores are produced in special organs of complex structure, called *sporangia*, which are borne in groups on the under surface of the leaves. In some ferns the sporangia are borne on the ordinary green leaves, but in other species there are two kinds of leaves: the ordinary green leaves, which bear no sporangia, and modified leaves called *sporophyls* which have little or no chlorophyl and whose sole function is to bear the sporangia. Within the sporangia are produced large numbers of sporocytes, each of which forms four haploid spores, just as in the mosses. When the spores are ripe, the sporangia open and scatter them.

Each spore develops, under favorable conditions, into a gametophyte. The fern gametophyte is a small, flat, heart-shaped, green plant, not more than a few millimeters in diameter, called a *prothallium*. These prothallia grow in moist places, on the ground or on decaying wood, and would never be recognized as "ferns" except by following the life history. The prothallium is self-supporting, containing chlorophyl and having rhizoids on its under surface for attachment and absorption. On the under surface of the prothallium, also, are the reproductive organs, *archegonia* and *antheridia*. Many ferns are monoecious, having both archegonia and antheridia on the same prothallium. These organs are quite similar to those of the mosses, described above. The sperm-cells of ferns are corkscrew-shaped, with a large number of flagella at the anterior end. When the antheridia are ripe they burst, liberating the sperms, which swim about in the moisture on the under side of the prothallia until they reach the archegonia; there is evidence of a chemotropic mechanism here, as in the mosses. The ferns are thus, like the mosses, dependent on water for fertilization, and can therefore flourish only in moist places.

After fertilization the zygote develops into the sporo-

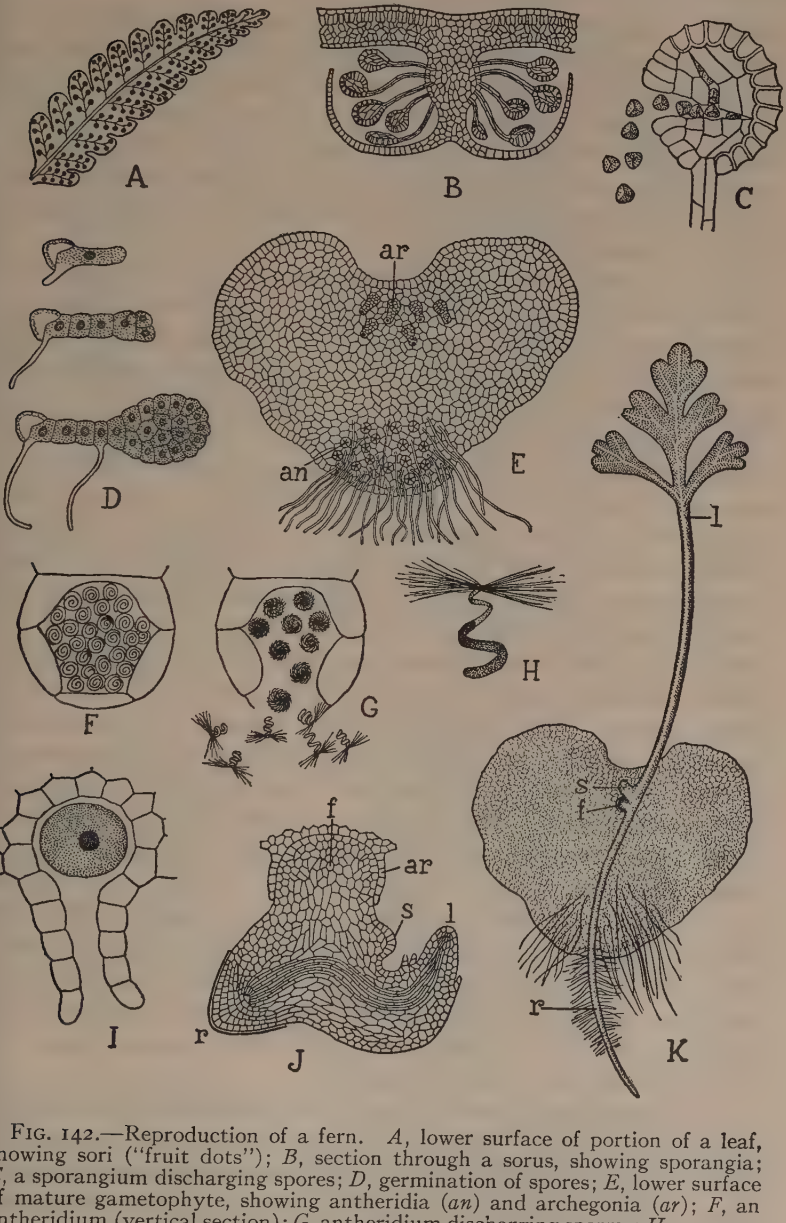


FIG. 142.—Reproduction of a fern. *A*, lower surface of portion of a leaf, showing sori ("fruit dots"); *B*, section through a sorus, showing sporangia; *C*, a sporangium discharging spores; *D*, germination of spores; *E*, lower surface of mature gametophyte, showing antheridia (*an*) and archegonia (*ar*); *F*, an antheridium (vertical section); *G*, antheridium discharging sperms; *H*, a sperm; *I*, a mature archegonium, showing the egg-cell (vertical section); *J*, embryo sporophyte, with its foot (*f*) embedded in the remains of the archegonium (vertical section); *K*, young sporophyte, still attached to the parent gametophyte; *r*, root; *s*, stem; *l*, leaf.

phyte. The embryo is at first enclosed within the archegonium, and draws its nourishment from the gametophyte by means of a *foot*, as in the moss. Shortly, however, the young sporophyte bursts the wall of the archegonium, sends a root down into the soil and a leaf up into the air, and becomes self-supporting. Soon afterward the gametophyte dies. The sporophyte may live for years, producing many crops of spores.

In the ferns, then, both generations are independent, autotrophic plants, but the sporophyte is much the larger, more complex, and longer-lived. As compared with the moss, the fern sporophyte is much more highly developed, but its gametophyte is smaller and simpler.

In some other pteridophytes, the gametophyte is still further reduced. These cases are interesting as affording a transition from the conditions in the ferns to those in the seed-plants. A good example of these pteridophytes with greatly reduced prothallia is the plant Selaginella. The sporophyte of this plant is a vascular plant, consisting of roots, stem, and leaves, but quite different from a fern in external appearance. It has a profusely branched creeping stem, with some short erect branches, and small scale-like green leaves. The sporangia are borne on specialized sporophyls, which are grouped to form cone-like structures at the tips of the erect branches. Each sporophyl bears a single sporangium. The larger sporophyls at the base of the cone, called *macrosporophyls*, bear large sporangia called *macrosporangia*. The *microsporophyls*, forming the upper part of the cone, bear smaller sporangia, called *microsporangia*. Each macrosporangium bears a single large sporocyte, producing four *macrospores;* each microsporangium produces many *microspores*. A macrospore is about ten times as great in diameter—*i.e.*, about a thousand times as great in volume—as a microspore.

The microspores develop into *male prothallia*, the macrospores into *female prothallia*. Both kinds of prothallia develop entirely within the spores, have no chlorophyl, and draw their nourishment entirely from food substances stored in the spores. The male prothallium consists of a single antheridium, producing a number of sperm-cells, which are liberated at maturity by the bursting of the

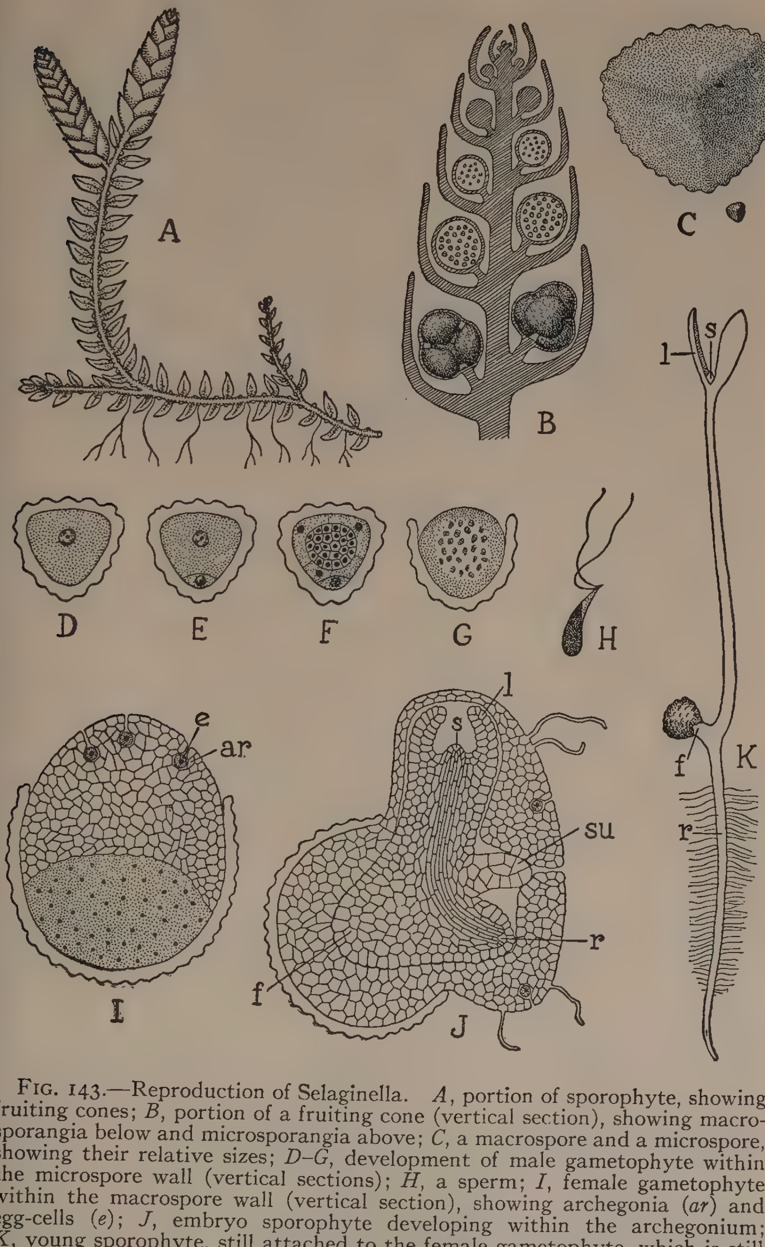


FIG. 143.—Reproduction of Selaginella. *A*, portion of sporophyte, showing fruiting cones; *B*, portion of a fruiting cone (vertical section), showing macrosporangia below and microsporangia above; *C*, a macrospore and a microspore, showing their relative sizes; *D–G*, development of male gametophyte within the microspore wall (vertical sections); *H*, a sperm; *I*, female gametophyte within the macrospore wall (vertical section), showing archegonia (*ar*) and egg-cells (*e*); *J*, embryo sporophyte developing within the archegonium; *K*, young sporophyte, still attached to the female gametophyte, which is still within the macrospore wall; *f*, foot; *r*, root; *s*, stem; *l*, leaf; *su*, suspensor.

microspore wall. The female prothallium consists of a mass of undifferentiated cells with a few archegonia at one end; at maturity the wall of the macrospore bursts at this end, exposing the archegonia. Each archegonium contains a single egg-cell, which is fertilized in the usual way. The embryo sporophyte begins its development within the archegonium, and draws its nourishment from the female prothallium, still within the old macrospore wall, until its first leaves and roots are formed.

In Selaginella (and a few other pteridophytes) the gametophyte has lost entirely the status of an independent, self-supporting plant, and is reduced to merely a reproductive mechanism. Not only the gametophyte but also the embryo sporophyte are nourished by food originally produced by the parent sporophyte and stored in the spores.

Spermatophytes.—This group comprises all plants reproducing by *seeds*. In these plants the sporophyte generation is the principal one, as in the pteridophytes, and the gametophyte is still further reduced. One small group of seed-plants, the gymnosperms—including the conifers (pines, cedars, etc.), the gingko tree, cycads, and a few others—presents an almost continuous series of transitions, in the reproductive mechanisms, between the conditions in Selaginella and those in the typical flowering plants, the angiosperms. We must here, however, pass over these interesting transition types, and confine our attention to the angiosperms, which include the great majority of familiar plants.

The plant body, consisting of roots, stem, and leaves, whose structure and nutrition have been previously described (pp. 163–183), is the sporophyte, with diploid nuclei. The reproductive mechanisms of the plant are located in the *flowers*. A flower is a group of modified leaves of several kinds. In a *complete* flower there are four distinct kinds of modified leaves, arranged in concentric whorls. The outermost whorl is called the *calyx*, its separate parts *sepals:* these are usually quite leaf-like in form and color. Inside the calyx is the *corolla*, whose separate parts are called *petals:* these are also leaf-like in form, but often brightly colored. The calyx and corolla together constitute the *floral envelopes;* they play no direct part in reproduction.

These parts are subject to endless variations, in different species of plants, in form, color, number of segments, etc., or either or both of them may be absent entirely. Next inside the corolla come the *stamens:* these are the *microsporophyls*, but so highly modified in form as to be quite unrecognizable as leaves. The innermost whorl consists of the *carpels*, which are the *macrosporophyls*, also quite unleaf-like in appearance. In most flowers all the carpels are united, partially or completely, to form a single compound organ called the *pistil.* These parts also vary in form and number in different species of plants. In most species each flower contains both stamens and carpels; but in some plants there are two kinds of flowers, one containing only stamens (*male* flowers), the other only carpels (*female* flowers). These two kinds of flowers may be borne on the same plant, or on separate individual plants; in the latter

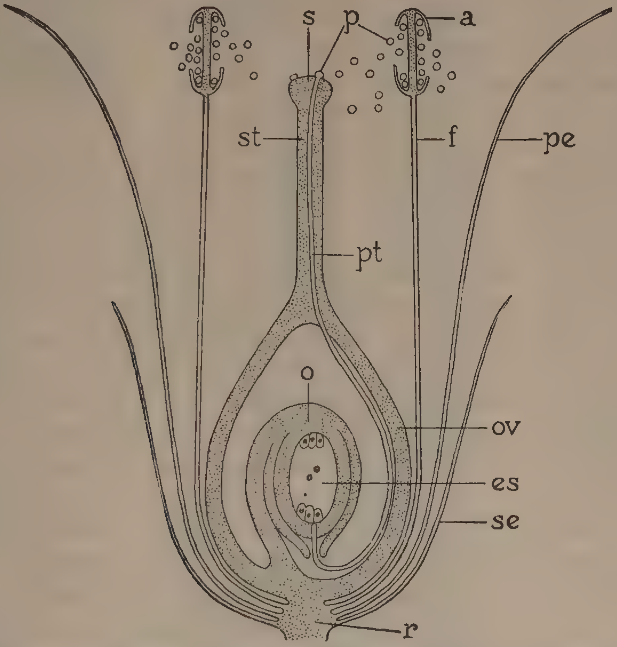


FIG. 144.—Diagrammatic longitudinal section of a mature flower, showing pollination. *r*, receptacle; *se*, sepal; *pe*, petal; *f*, filament; *a*, anther; *p*, pollen grains; *s*, stigma; *st*, style; *ov*, ovary; *o*, ovule; *es*, embryo sac (female gametophyte); *pt*, pollen tube (male gametophyte).

case, the plants bearing staminate flowers are male plants, those bearing pistillate flowers female plants. Thus sexual differentiation has extended back, so to speak, from the gametophytes to the sporophytes which produce them.

Each stamen consists of a slender *filament* bearing at its tip the *anther*, which is made up of several—usually two or four—*microsporangia*. Within these are formed the *microspores*, commonly called *pollen grains*. These spores are formed in the same way as in the bryophytes and pteridophytes; *i.e.*, from sporocytes, each of which undergoes synapsis and two maturation divisions, forming four spores. Each spore, or pollen grain, therefore has the haploid number of chromosomes in its nucleus. When the pollen is ripe, the pollen sacs (microsporangia) split open, liberating the pollen grains.

The pistil (or each carpel, when these are separate) consists of an enlarged hollow portion, the *ovary*, at the base, surmounted by a slender cylindrical portion, the *style*, which terminates in a moist, sticky surface, the *stigma*. Within the ovary are the *ovules*—from one to many in number, in different species—which are the *macrosporangia*. Within each ovule develops a single *macrospore*. This is produced from a sporocyte, by two maturation divisions, just as in the lower plants, but only one of the four cells thus produced becomes functional, the other three degenerating, as in the maturation of the animal egg. After the maturation divisions, the macrospore nucleus (which is, of course, haploid) usually divides three times, forming eight nuclei; its cytoplasm is usually divided into seven cells, three at each end and a large cell with two nuclei in the middle. This whole structure, called the *embryo-sac*, constitutes the female gametophyte; it remains completely enclosed by the integuments of the ovule (*i.e.*, the wall of the macrosporangium), within the ovary. One of the small uni-nucleate cells of the embryo-sac is the *egg-cell*. In some species of angiosperms the number of divisions of the macrospore nucleus, after the maturation divisions, is only one or two, instead of three; and in a few species there are no such divisions, one of the four nuclei resulting from the maturation divisions becoming the egg-nucleus directly, just as in animals.

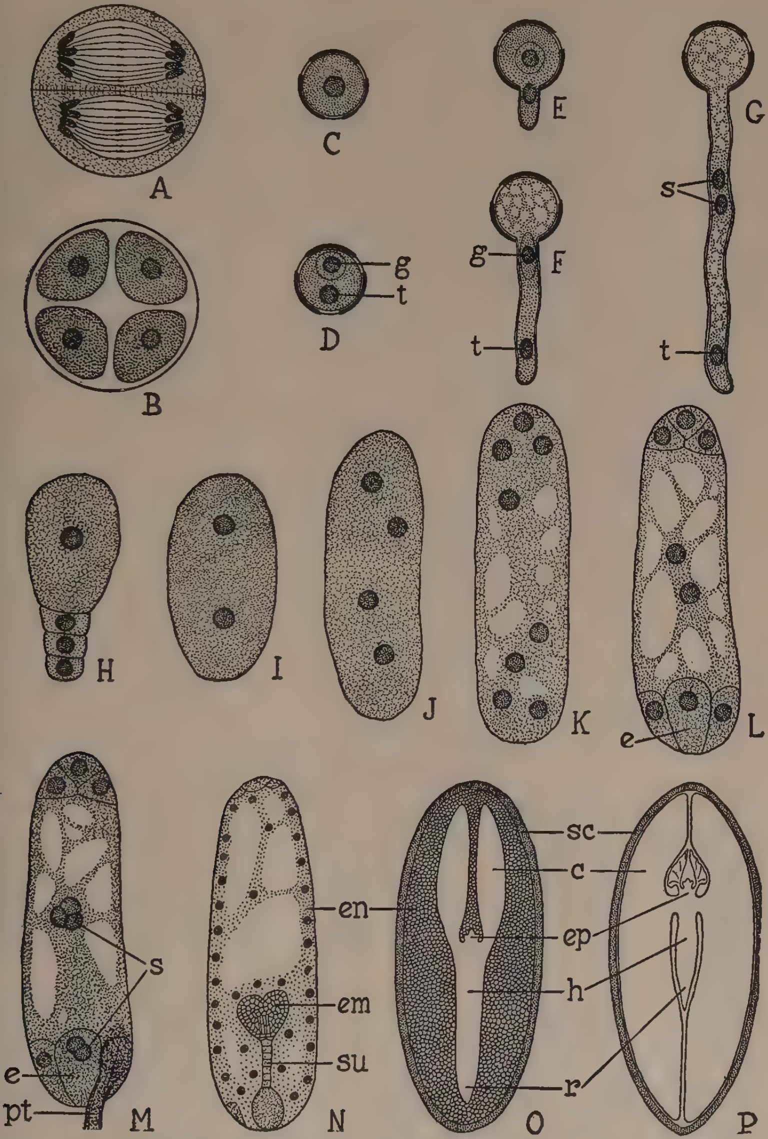


FIG. 145.—Reproduction of angiosperms. *A*, *B*, division of microsporocyte into four microspores (pollen grains); *C–G*, development of microspore into male gametophyte; *t*, tube nucleus; *g*, generative nucleus; *s*, sperm nuclei. *H*, the macrospore and its three sterile sister cells (corresponding to polar bodies), formed by division of the macrosporocyte; *I–L*, development of macrospore into female gametophyte; *e*, egg-cell. *M*, fertilization; *pt*, pollen tube; *s*, sperm nuclei. *N*, development of embryo (*em*) and endosperm (*en*); *su*, suspensor. *O*, a mature seed with endosperm; *P*, a seed without endosperm; *c*, cotyledon; *h*, hypocotyl; *ep*, epicotyl; *r*, radicle; *sc*, seed coats.

The pollen grains (microspores), after their liberation from the anthers, may light on the stigma of the same flower or of other flowers. In some species, *self-pollination* is the rule, the pollen falling directly on the stigma at maturity. In many plants, however, *cross-pollination* is the rule, the pollen being carried from one flower to others by the wind, water (in aquatic plants), insects, or birds. On the stigma, the pollen grains germinate (they will also germinate in a sugar solution), each grain producing a long slender tube which grows down through the tissues of the style and ovary to an ovule. The nucleus of the pollen grain (microspore nucleus) divides into two nuclei: one of these, the *tube nucleus*, does not divide again; the other divides once more, forming two *sperm nuclei*. The pollen tube, with its three nuclei, constitutes the male gametophyte. The tip of the pollen tube grows into the ovule (usually through a small pore, the *micropyle*), and into the embryo-sac. Here the end of the tube is ruptured and the two sperm nuclei are discharged into the embryo-sac. One of these sperm nuclei unites with the egg-cell nucleus, forming a diploid zygote nucleus, just as in all other sexually reproducing organisms. At the same time another nuclear fusion occurs which is peculiar to the angiosperms: the second sperm nucleus unites with the two nuclei of the large central cell of the embryo-sac, forming a *triploid* nucleus (containing n chromosomes from the sperm nucleus and n chromosomes from each of the two embryo-sac nuclei), called the *endosperm nucleus.* Immediately or shortly after fertilization the zygote (fertilized egg-cell) begins to divide, and develops into an embryo sporophyte, consisting of a minute root, stem, and one or two leaves, called *cotyledons*. At the same time, the endosperm nucleus also divides, and produces a mass of cells, called the *endosperm*, in which reserve food substances (starch, proteins, and sometimes fat) are stored. The whole structure thus formed is the *seed*, composed of: the *seed coats*, developed from the integuments of the ovule, which are tissues of the parent sporophyte; the *endosperm*, formed as described above; and the *embryo*, which is the young sporophyte developed from the fertilized egg-cell. In some seeds (*e.g.*, corn), the endosperm forms a large part of the mature seed, containing most of its stored food supply. In other seeds (*e.g.*, peas), most of the food material is stored in the cotyledons (leaves) of the embryo itself, and the endosperm is absent in the mature seed. While the seeds are being formed, the ovary (together, in some cases, with some other parts of the flower) develops into the *fruit*, which assumes a great variety of forms in different species of plants.

The development of the embryo ceases, temporarily, when the seed is ripe. The seeds are now liberated from the parent plant, either by the opening of the fruit—called, in these cases, a *capsule* or *pod* (*e.g.*, in peas, beans, etc.)—or by the detachment of the whole fruit (*e.g.*, nuts, berries, etc.). Sooner or later—usually in the following spring—the seed, under favorable conditions, *germinates; i.e.*, the embryo resumes growth and development. During the first part of its development the young plant derives its nutrition from the stored food substances in the endosperm or cotyledons. Soon after the stem and leaves appear above ground, chlorophyl develops in them and the plant becomes autotrophic.

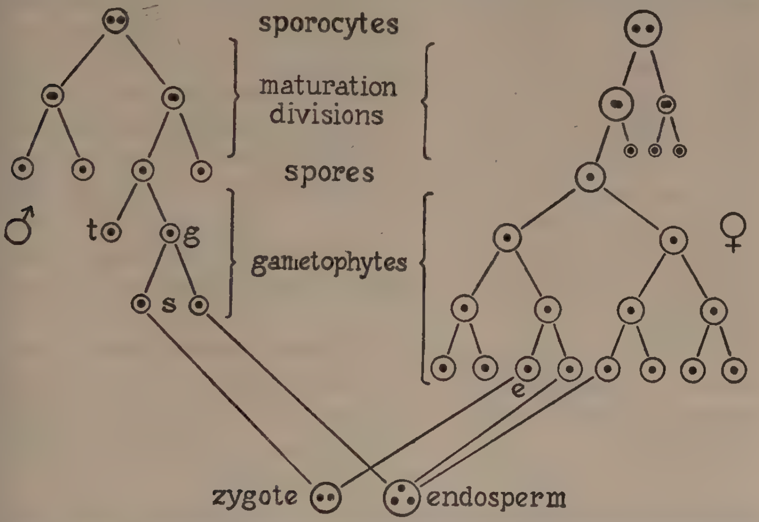


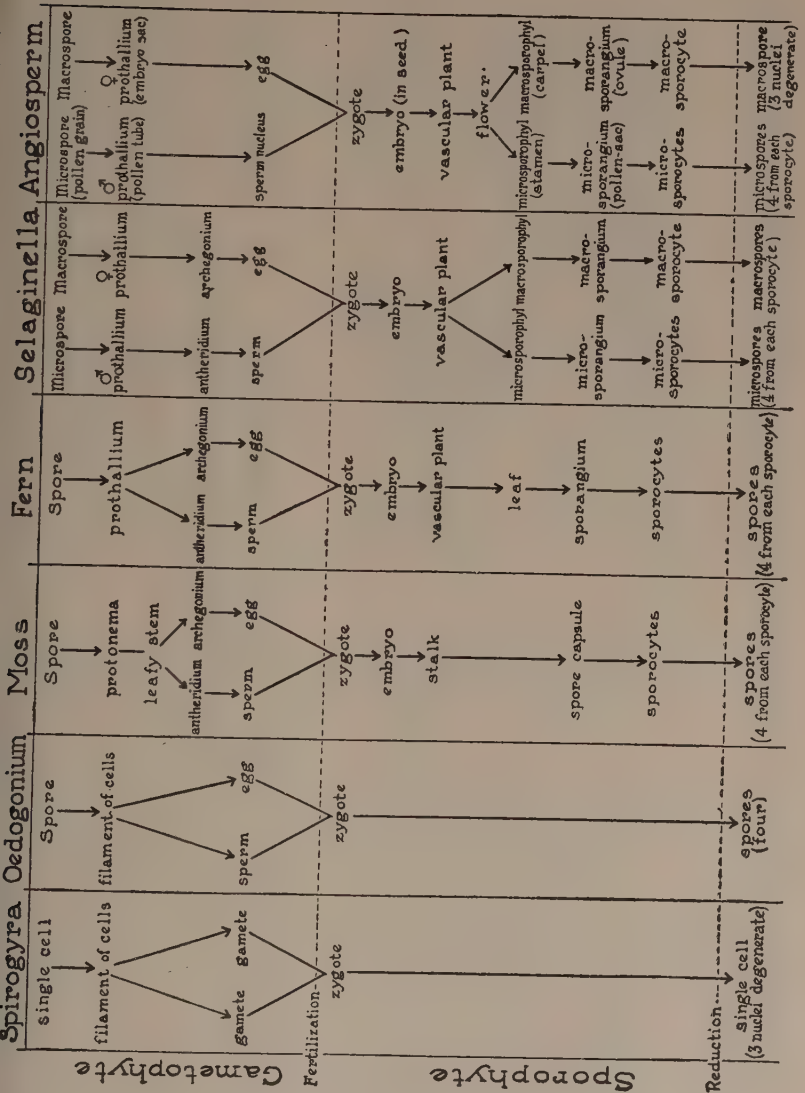
FIG. 146.—Diagram of spore formation, development of the gametophytes, and fertilization in angiosperms. One, two, and three dots indicate haploid, diploid, and triploid nuclei respectively. *t*, tube nucleus; *g*, generative nucleus; *s*, sperm nuclei; *e*, egg-cell.

In the spermatophytes, then, especially in the angiosperms, the gametophyte generation has almost entirely disappeared, being reduced to three cells in the male gametophyte and eight, or sometimes less, in the female (Fig. 146). The condition in these plants closely approaches that in animals, where all the cells except the gametes themselves are diploid. Along with this, sexual characters have extended back, so to speak, from the gametophyte to the sporophyte generation; *i.e.*, the sporophyte has what may be called male organs (stamens) and female organs (carpels), and in some species even separate male (pollen-producing) and female (ovule-producing) plants. Furthermore, not only the gametophytes but also the embryo sporophytes derive their nutrition from the parent sporophyte, to which they remain attached during their embryonic development. This phenomenon is comparable to viviparity in animals (p. 389), and effects the same result; *i.e.*, the young organism when detached from the parent is relatively well developed and its chance of survival is thereby greatly enhanced (p. 389).

Comparison of life cycles of plants.—From the simplest sexually reproducing plants (thallophytes) to the highest (spermatophytes) there is a gradual decline in the relative size and importance of the haploid, or gametophyte, phase and a corresponding increase in those of the diploid, or sporophyte, phase of the life cycle. The former, which in most algae comprises practically the whole plant, is reduced in the angiosperms to a few dependent and short-lived cells; while the latter, represented in many algae only by the fertilized egg-cell, comprises practically the whole body of the seed-plant. The sporophyte, originally a strictly asexual generation, comes to assume, in some pteridophytes (*e.g.*, Selaginella) and all spermatophytes, certain sexual characteristics, *i.e.*, differentiation between male and female organs or even, in some species, between male and female individuals.

The table on page 441 compares, schematically, the life cycles of a series of plants selected to illustrate these changes in the relations of the two generations, corresponding stages and structures being placed in the same horizontal line.

Growth and development.—The structural aspects of


Spirogyra
Oedogonium
Moss
Fern
Selaginella
Angiosperm
Gametophyte
Fertilization
Sporophyte
Reduction
single cell
filament of cells
gamete
gamete
zygote
single cell (3 nuclei degenerate)
Spore
filament of cells
sperm
egg
zygote
spores (four)
Spore
protonema
leafy stem
antheridium
archegonium
sperm
egg
zygote
embryo
stalk
spore capsule
sporocytes
spores (4 from each sporocyte)
Spore
prothallium
antheridium
archegonium
sperm
egg
zygote
embryo
vascular plant
leaf
sporangium
sporocytes
spores (4 from each sporocyte)
Microspore
Macrospore
♂ prothallium
♀ prothallium
antheridium
archegonium
sperm
egg
zygote
embryo
vascular plant
microsporophyl
macrosporophyl
micro-sporangium
macro-sporangium
micro-sporocytes
macro-sporocyte
microspores
macrospores
(4 from each sporocyte)
Microspore (pollen grain)
Macrospore
♂ prothallium (pollen tube)
♀ prothallium (embryo sac)
sperm nucleus
egg
zygote
embryo (in seed)
vascular plant
flower
microsporophyl (stamen)
macrosporophyl (carpel)
micro-sporangium (pollen-sac)
macro-sporangium (ovule)
micro-sporocytes
macro-sporocyte
microspores (4 from each sporocyte)
macrospore (3 nuclei degenerate)

development are, in general, simpler in plants than in animals. Most of the parts of the plant body are essentially solid structures, in contrast to the hollow and tubular organs of animals. The development of the plant body consists of cell divisions and growth, localized at certain points and unequal in different directions, producing the external form of the plant, and cellular differentiation producing the internal tissue structure, without the complex foldings, invaginations, and cell migrations characteristic of animal development (p. 392).

In all multicellular plants (except some of the simplest thallophytes with little or no cell differentiation) growth and cell division are confined largely or entirely to a *growing point* at the apex of each filament or lobe in the lower plants, or of each stem and root in higher plants. The cells of the growing point retain permanently the nature of undifferentiated, embryonic tissue, and continue indefinitely to produce new tissues and organs by growth and cell division. In many thallophytes, bryophytes, and pteridophytes, the apex of the growing point consists of a single large cell, called the *apical cell*, which, by continued growth and cell divisions, produces all the tissues of the plant. In the spermatophytes, a distinct apical cell can not be recognized, but the growing point consists of a conical mass of embryonic cells arranged in regular layers. This embryonic tissue is called *meristem*. Behind the growing point, the cells increase in size, largely by absorption of water, and become differentiated into the various mature tissues of the plant. The mature, differentiated cells usually have thick, often woody, cell walls, and are incapable of further growth and division. Contrasting the development of plants with that of animals, we may say, in a general way, that growth and differentiation in plants are *localized*—confined to certain parts of the body—but potentially *unlimited* in duration and magnitude, while in animals these processes occur throughout the body but are definitely limited, ceasing when a certain specific size and form have been attained.

These general features of growth and development are common to all differentiated multicellular plants. Some of the special features of development in particular groups of plants have been mentioned briefly in the preceding sections. We shall confine our attention here to the development and growth of seed-plants. More specifically, in those points in which there are differences among the several groups of seed-plants, the following account applies to the dicotyledons, the largest class of spermatophytes.

Immediately, or very shortly, after fertilization development is initiated by a series of cell divisions of the zygote.

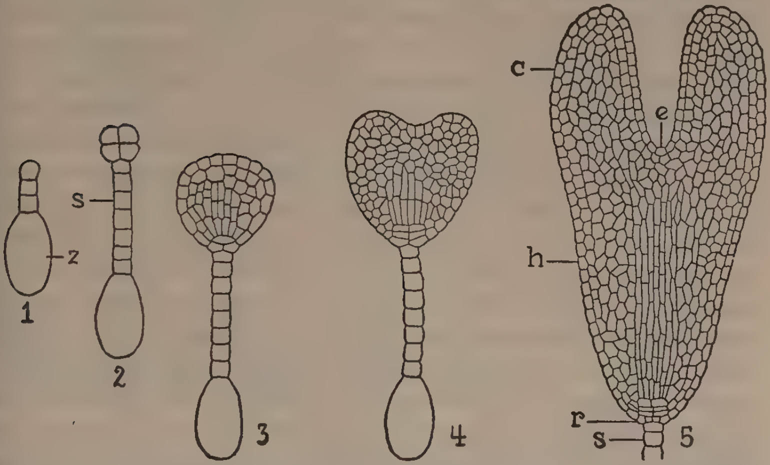


FIG. 147.—Development of a dicotyledonous embryo. *z*, original zygote cell; *s*, suspensor; *c*, cotyledon; *h*, hypocotyl; *e*, epicotyl; *r*, radicle. Later stages are shown in Fig. 145, *O* and *P*.

The first few divisions are all in planes perpendicular to the longest dimension of the embryo-sac, producing a filament of cells which grows out into the center of the embryo-sac. Then the terminal cell of this filament begins to divide in various planes, producing a solid spherical mass of cells, from which the whole of the embryo is formed, the basal portion of the original filament later degenerating. Growth and cell division become most rapid at two points on the free end of the embryo (*i.e.*, the end farthest from the original position of the egg-cell), resulting in two large outgrowths which become the *cotyledons*, or first leaves.[1] Meanwhile the rest of the embryo elongates, forming a cylindrical structure, the *hypocotyl*, or embryonic stem.

---

[1] In the monocotyledons there is only one cotyledon; in the gymnosperms there are usually several.

The end of the hypocotyl farthest from the cotyledons forms the *radicle*, or embryonic root, while the growing point of the stem, between the bases of the cotyledons, develops an embryonic bud, called the *epicotyl*. Simultaneously with the development of the embryo, the endosperm (whose origin has been previously described, p. 438) grows to fill all the space in the embryo-sac outside the embryo, while the integuments of the ovule become thicker and harder, forming the seed-coats. In some plants the growth of the embryo ceases while it still occupies but a small part of the seed, surrounded by a copious endosperm, but in others—*e.g.*, peas and beans—the cotyledons continue to grow until they have absorbed all of the endosperm.

When the seed is mature, development usually ceases temporarily. Some kinds of seeds are capable of germination as soon as they are mature, but most kinds will not germinate, even under the most favorable external conditions, until after a resting period of several weeks or longer. Some kinds of seeds are capable of surviving in this resting state for many years, though not indefinitely. The germination of the seed depends not only on its own condition of ripeness, but also on external factors, the most generally important of which are temperature and moisture. Under natural conditions, therefore, most seeds remain in the resting state throughout the winter or the dry season. With the advent of warmth and moisture, the seed absorbs water and swells powerfully, bursting the seed-coats, and the embryo resumes its growth and development. The radicle elongates rapidly, forming the primary root, which soon develops a zone of root-hairs near its tip. This primary root always grows downward, regardless of the original position in which the seed may happen to lie. It can easily be shown experimentally that this direction of growth is a response to the force of gravity; in other words, the primary root is positively geotropic (p. 336). At the same time, or slightly later, the primary stem grows upward; this is also a geotropic response, but in the opposite direction, *i.e.*, the stem is negatively geotropic; later the direction of growth of the stem is largely determined by its phototropic response, *i.e.*, it grows toward the light. In some plants, the hypocotyl elongates, pulling the cotyledons out of the seed and carrying them upward; in others, the cotyledons remain in the seed, only the epicotyl growing upward. During the process of germination, the young plant derives its nourishment from the reserve food material stored in the endosperm or the cotyledons, which is in part oxidized, in part converted into new protoplasm and cell walls; despite the fact that the amount of organic substances in the plant is decreasing, its size increases greatly, by the absorption of water. In some plants the cotyledons, as their stored food substances are used up, develop into ordinary foliage leaves; in others, they shrivel up and the first foliage leaves are developed from the stem above them. In either case, chlorophyl develops in the leaves, and also in the stem, shortly after they reach the light. With the development of chlorophyl in the stem and leaves and of root-hairs on the root, the young plant becomes self-supporting.

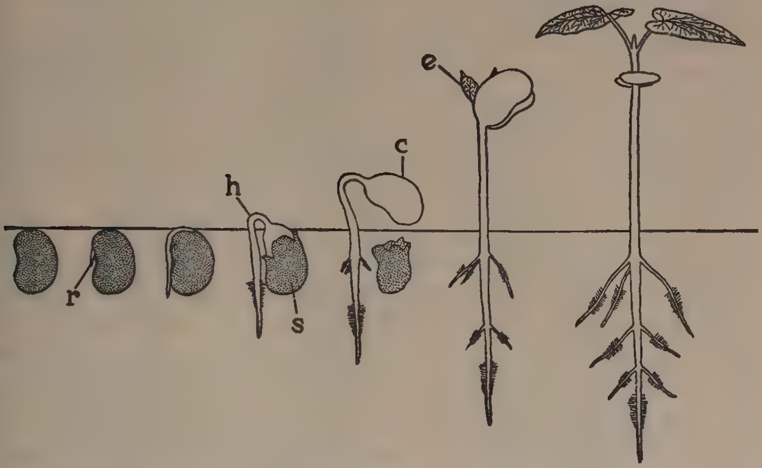


FIG. 148.—Germination of a seed (bean). *s*, seed coats; *r*, radicle; *h*, hypocotyl; *c*, cotyledon; *e*, epicotyl.

The further development of the plant is effected by the growth and cell divisions of the meristem, or embryonic tissue, located chiefly at the growing points of the stem and the root. The region of greatest increase in length of a stem or root is just behind its growing point; in this *zone of elongation* the cells greatly increase in size, chiefly by absorption of water, which accumulates in the large central vacuoles of the cells. Behind the zone of elongation most of the cells become differentiated, largely by modification of their cell walls, into the various mature tissues of the plant: the outer layer of cells forms the epidermis, the interior layers the cortex, fibro-vascular tissues, and pith. There remains, however, (in the dicotyledons) a layer of undifferentiated embryonic cells, the *cambium*, between the xylem and the phloem portions of the bundles (Fig. 47). These cambium cells continue to grow and divide, effecting continuous increase in thickness of the stem and root. The cambium cells produce, by division, new cells on both sides: those on the inner side of the cambium layer differentiate into xylem tissues; those on the outer side into phloem. In the spring, the xylem cells form mostly vessels (ducts), in the late summer mostly wood fibers, resulting in a series of concentric *annual rings* in the wood of perennial stems and roots.

Leaves always originate from the embryonic tissue of the growing point of the stem. They first appear as small conical protuberances, those nearest the apex of the stem being the youngest and smallest. The leaves usually grow more rapidly than the stem which produces them, so that the older embryonic leaves overarch and envelop the younger ones and the growing point of the stem: this whole structure is called a *bud*. Some buds remain at this stage, without further development, for some time, *e.g.*, the *winter buds* of trees; these resting buds are usually protected by specially modified *scale leaves* which envelop the younger embryonic leaves and the growing point. The growth of a leaf, unlike that of most stems and roots, is *limited; i.e.*, it ceases when the leaf has attained a definite size and form. A leaf usually continues to grow at its apex for a short time only, and then completes its development by further growth and differentiation of its basal region.

In many of the lower plants branches may originate by bifurcation of the growing point of the stem, but in the spermatophytes branches almost always arise in the axils of the leaves. The new stem originates as an outgrowth of the meristematic tissue in the angle between the base of the embryonic leaf and the growing point of the main stem.

While the new stem is still very small, embryonic leaves begin to be formed by its growing point, forming a *lateral bud*. Many of these lateral buds may remain dormant for a long time, and often never develop further unless the *terminal bud* of the main stem is cut off or otherwise destroyed. Those which do develop form new stems and leaves, in the same way as the main stem.

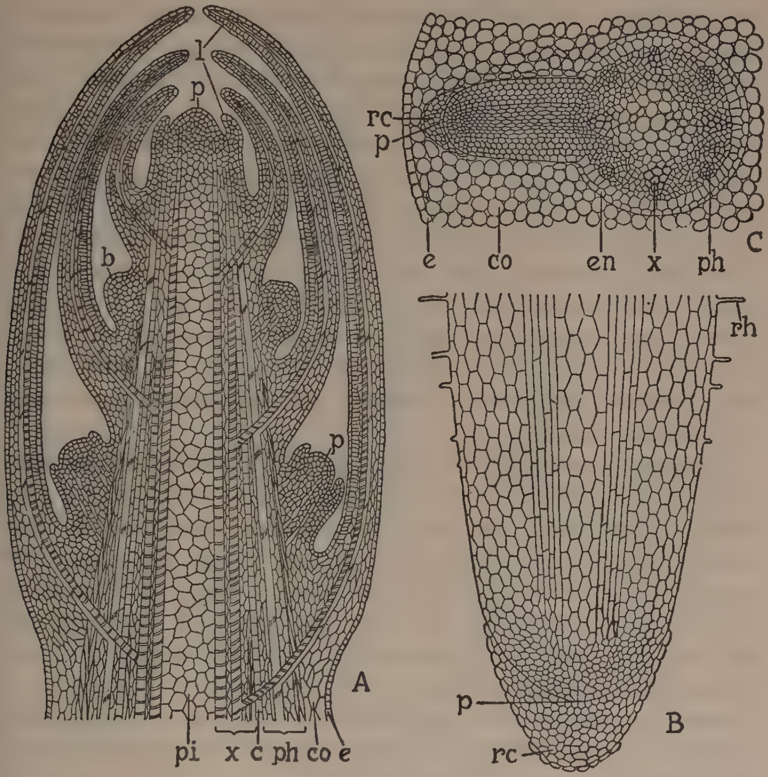


FIG. 149.—Growth of stems, leaves, and roots. *A*, longitudinal section of stem tip, showing origin of leaves and branches; *B*, longitudinal section of root tip; *C*, cross-section of part of older region of root, showing origin of a secondary root. *p*, growing points; *l*, leaves; *b*, origin of a branch (secondary stem); *pi*, pith; *x*, xylem; *c*, cambium; *ph*, phloem; *co*, cortex; *e*, epidermis; *rc*, root cap; *rh*, root hair; *en*, endodermis.

The growth of roots is quite similar to that of stems in most respects, but there are several differences by which stems and roots can always be distinguished. A root never bears leaves or buds. The growing point of a root is always covered by a *root-cap;* the cells composing the root-cap are continually worn away as the root pushes through the soil, and are replaced by others formed by the meristem of the growing point. The young epidermal cells of the root, a short distance behind its growing point, produce *root-hairs* (Fig. 50); as the older root-hairs die at the same rate that new ones are formed, only a small portion of the root, near its tip, is provided with root-hairs at any one time. The method of branching of the root is entirely different from that of the stem, new roots originating from the internal tissues of the old root at some distance behind the growing point. The new root arises from the fibro-vascular bundles of the parent root and grows out through the cortex of the latter. New roots may be formed in this way not only from the older roots but also from stems or even, in some cases, from leaves. Stems may also arise in this way, though usually only under abnormal conditions, from roots or from old stems.

Flowers develop at the ends of short stems of limited growth. The flower bud is formed in the same way as an ordinary leaf bud, the leaves becoming modified in the course of their development into sepals, petals, stamens, and carpels. The end of the floral stem, forming the base (*receptacle*) of the flower is usually flattened, so that the parts of the flower form concentric whorls, the center of the receptacle representing the tip of the stem.

Development of the germ cells.—The germ cells are those cells which are capable of reproducing the whole organism, and all cells from which these reproductive cells are, directly or indirectly, derived (p. 408). The special reproductive cells of plants are, as we have seen, of two kinds: gametes and asexual spores. In differentiated multicellular plants these reproductive cells are derived from the embryonic tissue, or meristem, of those parts of the plant where the reproductive organs are formed. We must logically regard all the undifferentiated cells of the meristem as germ cells, from which are derived, by cell divisions and differentiation, both somatic cells and specialized reproductive cells.

The *maturation* of the germ cells in *diploid* plants involves, as in animals, the complex chromosomal phenomena of synapsis and reduction. These processes are, in all essential respects, identical with those in animals, which have been previously described (p. 411). In every case there are, following synapsis, *two* maturation divisions, in the course of which the number of chromosomes in each nucleus is reduced from the diploid to the haploid number. In most cases the four cells produced by these two divisions are all functional; in some cases (p. 436) three of them degenerate and only one is functional. There is, however, in almost all plants, one important difference from animals: the cells resulting from the maturation divisions are not gametes but *asexual spores*. These develop, as we have seen, into haploid plants (gametophytes). Since the gametophyte has the haploid chromosome number in all its nuclei, there are no special chromosomal phenomena involved in the formation of the gametes, which are produced by ordinary mitotic divisions. To state this difference in another way: in animals the maturation divisions, resulting in reduction, are immediately followed by fertilization, restoring the diploid condition, while in most plants a number of haploid cell-generations intervene between reduction and fertilization. In the highest group of plants, the angiosperms, however, the number of successive nuclear divisions in the haploid (gametophyte) phase is very small: two in the male gametophyte and three, or sometimes less, in the female (Fig. 146); in a few cases there are no such divisions, *i.e.*, the cell resulting from the maturation divisions becomes directly the egg-cell, just as in animals.

Parthenogenesis and related phenomena.—Ordinarily, in all plants with a regular alternation of generations, the sporophyte develops from a fertilized egg-cell and has the diploid number of chromosomes in its nuclei, while the gametophyte develops from a spore produced by a reduction division and has the haploid chromosome number. In a number of species of pteridophytes and spermatophytes, however, there are exceptions to these general rules. In these cases, the sporophyte develops from the gametophyte asexually, either by parthenogenesis or by budding: these processes are called *apogamy*. In almost all cases where apogamy occurs naturally, the gametophyte in turn develops from the sporophyte without reduction, either from spores produced without a reduction division or by budding: these processes are called *apospory*. It is obvious that in these plants, since there is neither fertilization nor reduction, the sporophyte and the gametophyte have the same number of chromosomes. In some cases this is the haploid number; more frequently it is the diploid number.

Haploid parthenogenesis—the development of an unfertilized egg-cell with the haploid number of chromosomes—is not known to occur naturally in any of the higher plants (it may occur in some algae), but it has been induced experimentally in some cases, producing haploid sporophytes. In a number of species of ferns, haploid sporophytes develop from the gametophytes by a process of budding; *i.e.*, the sporophyte develops directly from the tissues of the gametophyte without any egg-cell.

Diploid parthenogenesis occurs in a number of species of pteridophytes and spermatophytes. In such plants the gametophyte is diploid, the egg-cell therefore has the diploid number of chromosomes and develops directly into a sporophyte without fertilization. In some other species with diploid gametophytes the sporophyte develops directly from the gametophyte by a process of budding, without any egg-cell. The diploid gametophyte is produced in either one of two ways: from a diploid spore produced by the sporophyte without a reduction division, or by budding from the tissues of the sporophyte without any spore. Diploid gametophytes have also been produced experimentally in a number of mosses from diploid cells of the sporophytes.

These cases show that while the gametophyte is ordinarily haploid and the sporophyte diploid, they are *not necessarily* so; *i.e.*, we can not say that one generation is the gametophyte *because* it has the haploid number of chromosomes in its nuclei, or that the other is the sporophyte *because* it has the diploid number.

Budding, fission, and regeneration.—Multiplication by budding or fission—*i.e.*, the production of new individuals from multicellular portions of the parent plant, without any special reproductive cells—is of frequent occurrence among all groups of plants. These processes are commonly called *vegetative reproduction*. There is a great variety of mechanisms, in different plants, by which this is effected. In some cases a special kind of buds, called *bulbils* or *gemmae*, are formed and detached from the plant, each developing into a new plant; this occurs in many species of bryophytes, pteridophytes, and spermatophytes. Other plants (*e.g.*, the strawberry) produce long *runners*, or prostrate stems, from the buds of which new plants develop. In other cases new plants arise from the buds of underground stems: the *tubers* of the potato and some other plants are specialized types of underground stems by which the plant multiplies vegetatively. *Bulbs*, which are underground buds, produce new bulbs in the axils of their scale leaves, and each of these new bulbs may develop into a separate plant. In a number of ferns, and also some seed-plants, new plants may arise by a process of budding from the leaves. The vegetative multiplication of the gametophyte in mosses has been described previously (p. 429).

Closely related to these methods of reproduction is the power of regeneration which is possessed to a high degree by most plants. It is a familiar fact that a *slip* or *cutting*—*i.e.*, a piece of the stem—of a plant can often form roots and develop into a new plant. In some plants a leaf, or portion of a leaf, can similarly give rise to a new plant. In some cases a few cells, or even a single cell, removed from a plant can produce a whole new plant. The opposite process, the combination of portions of two plants to form a single plant, called *grafting*, can also be effected in many plants, and is widely practiced with fruit trees.

A number of plants—*e.g.*, the banana, some varieties of other cultivated fruits, as well as some species of wild plants—have lost entirely the ordinary methods of reproduction, and are propagated solely by vegetative methods. These cases emphasize the fact, also demonstrated by many lower organisms (p. 378), that sexual reproduction is not essential for indefinitely continued life and multiplication.

CHAPTER XXII

HEREDITY

In the development of any individual organism from an original cell or group of cells (*e.g.*, a zygote, a parthenogenetic egg, a spore, or a bud), we may recognize two groups of factors operating to produce the observed results: external, or *environmental*, factors which may affect the organism in one way or another during its development; and internal factors present in the original cell (or cells), or, as we might say, the *original nature* of the organism itself. These initial internal factors, determined by the origin, or *descent*, of the organism, are called *genetic* or *hereditary* factors; their transmission from generation to generation—from parents to offspring—is called *heredity*. The processes by which these hereditary factors, in conjunction with environmental factors, produce the structures and other characteristics of the organism constitute *development*. In the present chapter we are concerned solely with heredity, as here defined—the transmission of hereditary factors. The problems of the mechanism of development will be discussed in the following chapter.

The mechanism of heredity.—Every individual organism, we have learned, originates as a portion of protoplasm—unicellular or multicellular—derived from one or two preexisting organisms by processes of cell division and, in sexual reproduction, cell fusion. Heredity is a consequence of this continuity of living substance from parents to offspring through cell division and fertilization. It has been noted several times in the preceding chapters that every differentiated multicellular organism consists of two classes of cells: *germ cells*, which are potentially capable of producing new organisms, and *somatic cells*, which have not this power. Since the original cell (zygote or spore) of each organism is a germ cell, and the germ cells can be, in some cases at least, visibly distinguished from somatic cells throughout development, we regard all cells in the line of descent of the reproductive cells as germ cells, and say that germ cells can produce both somatic and germ cells, but somatic cells can produce only somatic cells (p. 408). While this distinction is, in a sense, only a matter of definition, it nevertheless serves to emphasize an important fact:

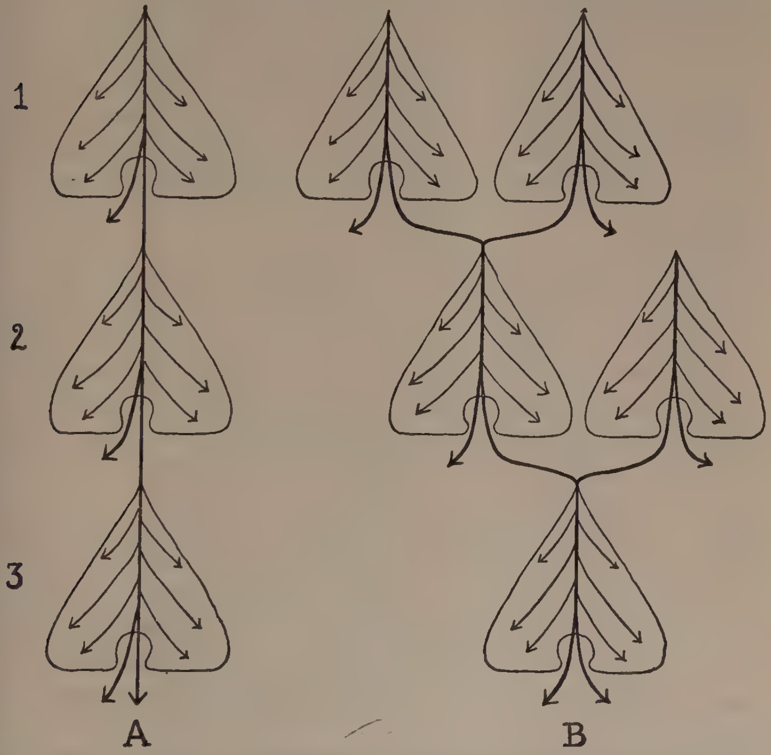


FIG. 150.—Diagrams illustrating the relation between germ plasm and soma: *A*, in asexual reproduction; *B*, in biparental sexual reproduction. *1*, *2*, *3*, successive generations. Heavy lines represent the germ plasm, light lines the soma produced by it in each generation.

that the germ cells of each generation are descended, by an unbroken series of cell divisions, from those of the previous generation; this is called the *continuity of the germ plasm*. The germ plasm is a series of cells which goes on, potentially forever, by cell division and fertilization, producing in each generation a group of differentiated and variously specialized cells, the *soma* or body, as well as more germ cells. The soma, in all complex organisms, completely surrounds the germ cells, protecting and nourishing them; sooner or later it dies, but meanwhile some of the germ cells may have become detached and produced new individuals. From the standpoint of the race, the soma is simply a vehicle for the germ plasm—"a hen is only an egg's way of making another egg." The similarities between parent and offspring—*i.e.*, between the soma of one generation and that of the next generation—are due to exactly the same cause as the similarities between two offspring of the same parent: to the fact that they are both derived from the same stock of germ plasm. Heredity is solely a function of the germ cells, though its *results* are usually *visible* only in the somatic cells, *i.e.*, in the structure and activities of the organism.

In all of the higher organisms, as we have seen, the two kinds of gametes are very unequal in size, the egg-cell being commonly thousands of times as large as the sperm. Despite this, the two gametes are, in general, equivalent in heredity; *i.e.*, an organism shows, on the average, as many hereditary characteristics of its father as of its mother. The only component which is equal in amount in the two gametes is the *chromatin;* moreover, the head of the sperm, which is often the only part that enters the egg in fertilization, consists almost entirely of chromatin (p. 387). These facts immediately suggest that the chromatin is particularly concerned in heredity. All the facts of heredity, indeed, as we shall see in the following pages, demonstrate conclusively that, with a very few exceptions, all the genetic factors of organisms, which determine their hereditary characteristics, are located in the chromatin of their nuclei. The chromatin, as we have learned, has a definite and complex organization, which is very constant and characteristic in all the cells of any one kind of organisms. At the time of mitotic cell division especially, the chromatin can be clearly seen to consist of definite bodies, of characteristic number, size, and shape, the *chromosomes*. Each chromosome, moreover, has a persistent individuality, reproducing itself by division in each cell-generation, and being transmitted regularly from cell to cell throughout the development of the organism, and from parent to offspring through the germ cells. The organization of the chromatin, however, is much more complex than this visible structure, for the phenomena of heredity demonstrate, as we shall see in the following pages, that each chromosome is composed of a large number of qualitatively different particles, arranged in a definite and constant order in the chromosome. These ultramicroscopic particles, called *genes*, are the ultimate agents of heredity—the individual hereditary factors. The mechanism of heredity, therefore, consists of the processes by which the genes are transmitted from cell to cell and from parent to offspring. These processes—mitosis, maturation of the germ cells, and fertilization—have already been described in some detail in the preceding chapters. We have seen that the most significant feature of ordinary mitotic division is the exact quantitative and qualitative division of each chromosome, and the equal distribution of the resulting daughter chromosomes to the two daughter cells. The method of division of the chromosomes—longitudinally—is such as to divide each individual gene into two, because the genes are arranged in a linear order (*i.e.*, in a single line, like beads on a string) in each chromosome. The result of this regular division and distribution is that all cells derived from a single original cell by ordinary mitotic divisions have exactly the same set of genes. Therefore all the cells of any individual organism (except the cells resulting from the maturation divisions) are identical in their hereditary constitution, and so are all organisms produced from a single ancestor by processes not involving reduction or fertilization, *e.g.*, by fission or budding. In sexually reproducing organisms, however, certain other processes come in to interrupt the regular series of mitotic divisions and modify the hereditary constitution of the offspring. At fertilization, as we have seen (p. 391), each gamete contributes a complete haploid set of chromosomes, which remain distinct and are distributed to all cells of the new organism. Each diploid cell of a sexually produced organism therefore contains two complete sets of genes, one set from each parent. At the maturation of the germ cells of such an organism, the chromosome number is reduced, each mature germ cell (gamete or spore) receiving only the haploid number of chromosomes. The distribution of the chromosomes to these cells at the reduction division is such

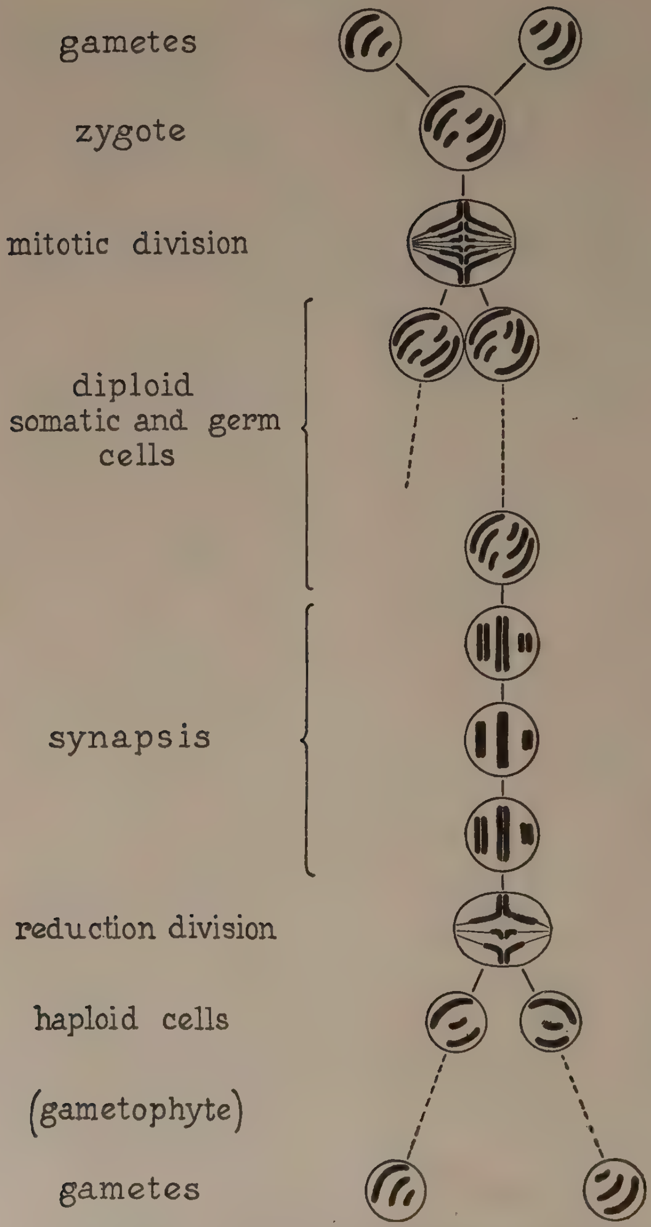

gametes
zygote
mitotic division
diploid somatic and germ cells
synapsis
reduction division
haploid cells
(gametophyte)
gametes

Fig. 151.—Diagram of the chromosome cycle in sexually reproducing organisms. In this diagram the haploid number of chromosomes is three, and these are distinguished from each other by differences in length. For simplicity the reduction process is represented, in this and subsequent diagrams, as a single division.

that each cell receives one complete haploid set, *i.e.*, one member of each pair of homologous chromosomes (p. 413). These haploid sets, however, are not necessarily, or usually, identical with those which combined originally to form the zygote; *e.g.*, if the chromosomes derived originally from the mother through the egg-cell be designated A, B, C, and those derived from the father through the sperm a, b, c, the gametes of the offspring may receive A, B, c, or A, b, c, or a, B, c, etc. It can easily be calculated that the number of different combinations of this kind is 2^n, where n is the haploid number of chromosomes. The number of genetically different gametes (or spores) produced by a diploid organism may, however, be much larger even than this, for the *individual chromosomes* of the mature germ cells are not always identical in composition with those of the diploid cells of the organism. This is due to the process of *synapsis*, which precedes the maturation divisions (p. 411): in some cases, the two chromosomes of a synaptic pair may exchange material with each other during this process, so that the two homologous chromosomes which separate at the reduction division may each contain some genes of chromosome A and other genes of chromosome a. In this case the possible number of genetically different gametes which could be produced by a diploid organism is 2^x, where x is the total number of genes in one haploid set of chromosomes. As x is probably usually in the thousands, it will be seen that the number of genetically different gametes which might be produced by any individual organism is extremely large. From this it results that, in sexually reproducing organisms, neither parent and offspring nor the several offspring of the same parents are, in general, identical in hereditary constitution. It is important to realize clearly that the mechanism of heredity is responsible for *differences*, as well as *similarities*, among individuals related by descent.

Methods of studying heredity.—The phenomena of heredity are studied by the method of *experimental breeding*. This consists in crossing—*i.e.*, mating together—individuals which differ from each other in one or more characteristics determined by hereditary factors, and studying the distribution of these characteristics in their offspring and in subsequent generations derived from these offspring by various types of matings. The essential point in this method is the study of *single hereditary differences*, separately or in combination, by *counting* the number of individuals, among the offspring of each mating, which display each particular hereditary characteristic or each combination of such characteristics. In this way it is possible to trace the transmission of individual genetic factors from generation to generation, by means of the visible characters which they determine. Not all characters of an organism are equally suitable for such study, for in many cases the effects of one genetic factor may be obscured by those of others or of environmental factors. It is necessary, in order to obtain simple, easily explainable, results, to study first such characters as display clearly the effects of single hereditary factors; these results can then be used to disentangle the more complicated phenomena in other cases.

By these methods, it has proved possible to formulate the phenomena of heredity in a small number of rather simple and very exact generalizations, which are called the *laws of heredity*. The first two of these laws (Segregation and Independent Assortment) are called Mendel's laws. These two laws were first discovered in 1865, but their significance was not generally appreciated until 1900. The remaining laws have been discovered since 1910. It has also been shown, in this modern period, that the laws of heredity can be adequately explained in terms of the visible mechanism of heredity—the behavior of the chromosomes in mitosis, maturation, and fertilization. This explanation is called the *chromosome theory of heredity*.

The phenomena of heredity have been studied most extensively in multicellular animals (especially insects and vertebrates) and seed-plants; *i.e.*, in sexually reproducing organisms whose somatic cells are diploid. All the statements in this chapter refer to such organisms, except where otherwise specified. In other kinds of organisms, and in other methods of reproduction, the results differ in accordance with the differences in behavior of the chromosomes in these cases.

Segregation.—Mendel's first law of heredity is illustrated in the simplest manner by crossing two individuals which have a single hereditary difference. For example, the plant called the Four-o'clock (*Mirabilis jalapa*) has two races which differ only in the color of their flowers: in one race the flowers are red, in the other white. If we cross these two races, by transferring pollen from a red flower to the stigma of a white flower, or vice versa, all the offspring have pink flowers; that is, their flower color is intermediate between those of the two parents. We speak of the parents as the *P1* (first parental) generation, and the offspring as the *F1* (first filial) generation. If we now *self-pollinate* any one of the *F1* plants, we get three kinds of plants in the next, or *F2*, generation: 25% of these plants have red flowers, like one of their grandparents, 25% have white flowers, like the other grandparent, and 50% have pink flowers, like the *F1* (all the flowers on any one plant being alike in every case). We next self-pollinate one or more plants of each of these three classes, with the following results: all the offspring (*F3*) of the red-flowered *F2* plants also have red flowers, the white-flowered plants give only white-flowered offspring, while the pink-flowered *F2* plants give the same result as the *F1* plants, *i.e.*, three kinds of offspring, in the proportions of 1 red-flowered: 2 pink-flowered: 1 white-flowered. We may continue thus indefinitely, always with the same results: red-flowered plants, self-pollinated, give only red-flowered offspring, white-flowered plants likewise give only offspring like themselves, while pink-flowered plants always give the three kinds of offspring in the proportions of 1 : 2 : 1. Exactly the same results are obtained if instead of self-pollinating the plants we cross any two plants of the same kind, *e.g.*, transfer pollen from one pink-flowered plant to the stigma of a flower on another pink-flowered plant.

We may take another example from animals. If we cross a White Andalusian fowl to a Black Andalusian (*i.e.*, mate a hen of either breed to a cock of the other), the offspring (*F1*) are all so-called Blue Andalusians,[1] whose feather color is intermediate between those of the two parents (the "blue" color being due to a less dense distribution of black pigment than in the Black race). Here we are dealing with dioecious organisms, which cannot self-fertilize, so we *inbreed* the *F1* fowls, *i.e.*, mate brother to sister. The results are precisely as in the previous example: 25% of the *F2* are white like one grandparent, 25% black like the other grandparent, and 50% blue like the *F1*. Continued inbreeding gives the same kind of results as in the previous example: blacks inbred give only black offspring, whites only white, while blues give always 1 black : 2 blue : 1 white.

---

[1] Only these "blue" birds are usually called Andalusians, but we shall here, for convenience, use this term also for the black and the white birds from which the blue hybrid is derived.

Similar results are always obtained in any *one-factor cross*, *i.e.*, a cross between two races having only *one hereditary difference*, provided the characters are such that the three classes—the two pure races and the hybrid—can be clearly distinguished. These results can all be explained by the simple hypothesis that the observed differences are due entirely to the effects of a *single pair of genes* located in one particular *pair of homologous chromosomes*. In the Black Andalusian fowl, for instance, there is, in *each* chromosome of a particular pair, in every cell, a gene which we may designate *B;* these genes determine the development of black pigment in the feathers. In the white race there is, in each chromosome of the same pair, instead of the gene *B* a different gene which we shall call *b;* because of this single genetic difference the feathers are white instead of black. At the reduction division, in the maturation of the germ cells of these animals, one chromosome of this pair goes to each haploid gamete nucleus; every gamete of the black race therefore contains one gene *B*, and every gamete of the white race contains one gene *b*. When these two races are crossed, each zygote therefore contains one gene *B* and one gene *b*, in homologous chromosomes derived from the egg-nucleus and the sperm-nucleus respectively. By the mechanism of mitotic division, every diploid cell of the animals developed from these zygotes contains *B* and *b*, and this *combination* determines the intermediate "blue" color of the feathers. At the reduction division, in the maturation of the germ cells of these *F1* animals, one chromosome of this pair goes to each haploid gamete nucleus; since one of these chromosomes (that derived originally from the black parent) contains the gene *B*, while the other (derived from the white parent) contains *b*, half of the gametes contain the gene *B*, the other half contain *b*. This is true of both the male and the female gametes—sperms and eggs. When these *F1* animals are inbred, any egg-cell

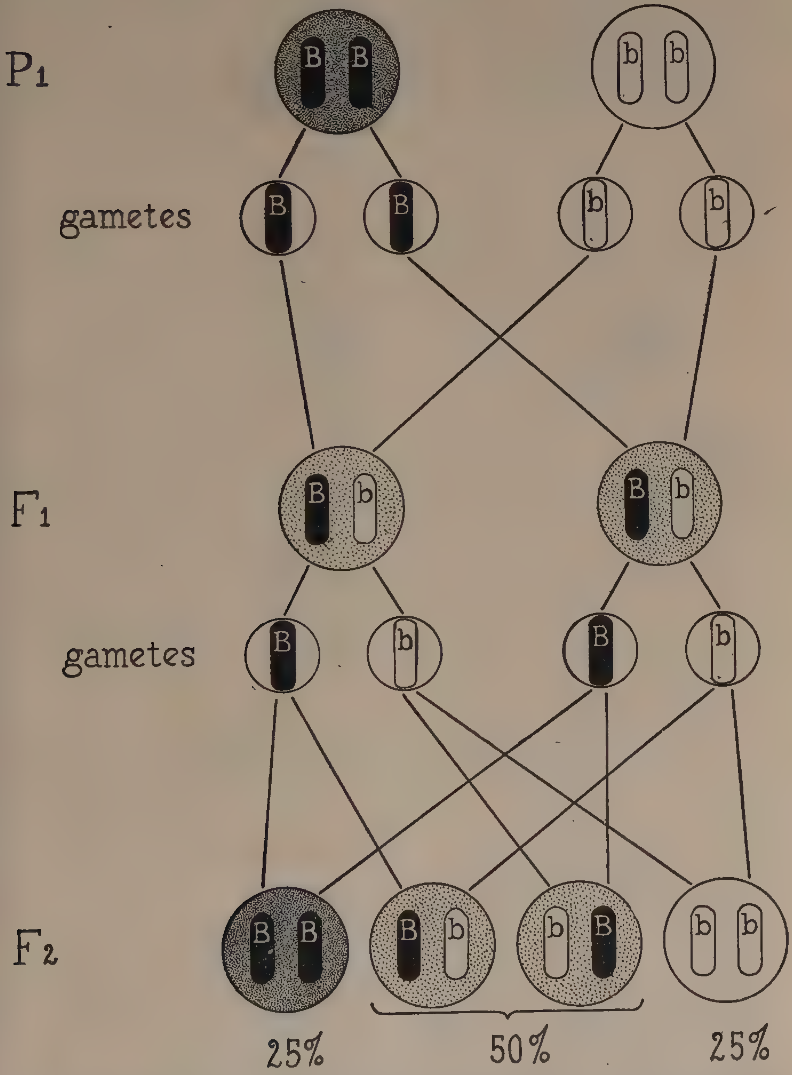


FIG. 152.—Diagram illustrating the cross of Black and White Andalusians and the inbreeding of their offspring (Blue Andalusians). The shading of the large circles indicates the color of the fowls. The straight rods represent the chromosomes, and the letters the genes, involved in the inheritance of this color. The two homologous chromosomes carrying different genes are colored differently in the diagram to distinguish them. The same conventions are used throughout the subsequent diagrams of this chapter.

may be fertilized by any sperm: therefore, on the average, half of the *B* eggs will be fertilized by *B* sperm, the other half by *b* sperm; similarly, half of the *b* eggs will be fertilized by *B* sperm, the other half by *b* sperm. The result will be 25% *BB* zygotes, 50% *Bb* zygotes, and 25% *bb* zygotes; consequently 25% of the *F2* animals are black, 50% blue, and 25% white. This may be made clearer by the following diagram:

F1 eggs	*B*	*b*
F1 sperms *B*	*BB* black	*Bb* blue
b	*Bb* blue	*bb* white

}*F2* zygotes

Inbreeding any of the black (*BB*) *F2* animals can give only black offspring, since these animals produce only *B* gametes; similarly the white (*bb*) animals produce only *b* gametes and give only white offspring when inbred; while the blue (*Bb*) *F2* animals produce both kinds of gametes in equal numbers, like the *F1*, and therefore give the three kinds of offspring in the proportions of 1 black (*BB*) : 2 blue (*Bb*) : 1 white (*bb*). The same kinds of results are repeated in every subsequent generation.

Exactly the same explanation applies in the case of the plant, the few haploid mitoses between reduction and fertilization (Fig. 146) making no difference in the results, because each gene present in the spore is divided and distributed to the two daughter nuclei at each of these divisions just as in diploid mitoses.

This explanation can be further tested by making other types of matings. If, instead of inbreeding the Blue Andalusians, we cross one of them to a Black, half the offspring are black and half are blue; if we cross a Blue to a White, half the offspring are white and half are blue. These results, it is readily seen, confirm the conclusion that the blue fowl produces equal numbers of *B*-containing gametes and *b*-containing gametes: when crossed to a black fowl, all of whose gametes contain the gene *B*, half the zygotes are *BB* (giving black feathers) and half are *Bb* (giving blue

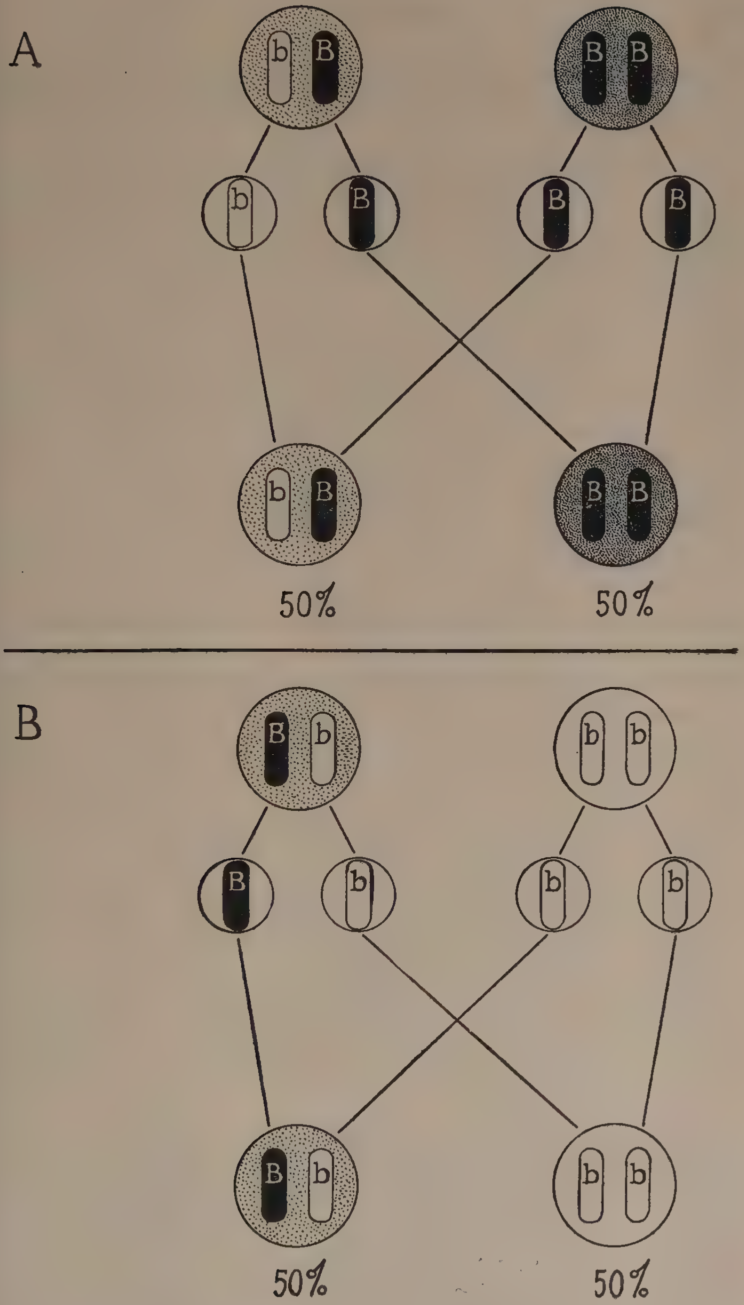

A
b B
B B
b
B
B
B
b B
B B
50%
50%
B
B b
b b
B
b
b
b
B b
b b
50%
50%

FIG. 153.—*A*, cross of Blue and Black Andalusians; *B*, cross of Blue and White.

feathers); when crossed to a white fowl, all of whose gametes contain *b*, half the zygotes are *bb* (white) and half are *Bb* (blue).

The two genes of a pair, such as *B* and *b* in the Blue Andalusian fowl, are called *allelomorphs*. All the genes of diploid organisms are in such pairs, the two allelomorphs of each pair being located in the two members of a pair of homologous chromosomes. An individual in which the two genes of an allelomorphic pair are alike (*e.g.*, *BB* or *bb*) is said to be *homozygous* for this pair of genes; an individual in which the two genes of an allelomorphic pair are different (*e.g.*, *Bb*) is called *heterozygous*. The Black and the White Andalusians, the red-flowered and the white-flowered Mirabilis are homozygous; the Blue Andalusian and the pink-flowered Mirabilis are heterozygous.

The separation of the two allelomorphic genes at the reduction division is called *segregation*. The results of *all* experiments such as those described above are summarized in the general statement called the Law of Segregation: *the two genes of an allelomorphic pair always segregate into separate germ cells at maturation, each allelomorph being entirely uncontaminated by the other*. As this law applies to every pair of allelomorphic genes, each mature (haploid) germ cell contains one, and only one, member of each pair of allelomorphic genes in the organism. Since all the genes of diploid cells are in allelomorphic pairs, this law applies to all the genes of all organisms which have a reduction division at any stage of their life cycle (*i.e.*, all sexually reproducing and some parthenogenetic organisms). Segregation occurs in homozygous as well as in heterozygous individuals, although its results are not so apparent in the former because all their gametes are alike, *i.e.*, contain identical genes.

The greatest significance of the Law of Segregation is that the genes do not in any degree "mix" with each other: although the visible characters of the organism (*e.g.*, its color) may show the effects of both allelomorphs, the genes themselves are entirely *uncontaminated* by each other; *e.g.*, the gene *B* in those gametes of a Blue Andalusian which contain it is exactly the same as in the gametes of the black race, and the gene *b* in gametes of the blue race is exactly the same as in the white race. The genes act as *stable, self-perpetuating units*, and heredity is simply the transmission of these units from generation to generation, forming ever new combinations by segregation and fertilization. Heredity, we may say, is a process of "shuffling," not "mixing"; or, in more technical language, heredity is *particulate*—a process of transmission of discrete, independent particles, the genes.

In the preceding paragraphs we have spoken of certain genes, or combinations of genes, as "determining" certain somatic characters of an organism, *e.g.*, the color of a fowl. By this we mean merely that of three fowls having respectively the genes *BB*, *Bb*, and *bb*—all other genetic factors and all environmental factors which might affect the color being identical in all three—the first will be black, the second blue, and the third white. The genes are *differential factors; i.e.*, a *difference* in these particular genes results in a *difference* in color. How these genes produce these effects is another question—a question not of heredity but of the mechanism of development, which will be discussed in the next chapter. So far as the study of heredity is concerned, the visible characters may be regarded merely as indicators of the presence of certain genes in the organism.

For the examples used above, we have deliberately chosen, for simplicity of understanding, cases in which the three classes—the heterozygous and the two homozygous classes—are easily and sharply distinguishable in appearance. This is, however, by no means always the case. It very frequently happens that the heterozygotes (*i.e.*, heterozygous individuals) are somatically indistinguishable from one of the homozygous classes, and can only be identified by genetic tests, *i.e.*, by breeding experiments. An example of this kind is seen in the cross of two races of peas having yellow and green seeds respectively. When these two races are crossed, *all* the *F1* seeds are *yellow*, just like those of the pure yellow-seeded race, with no apparent influence of the other parent. In this case the gene derived from the yellow-seeded race (which we shall call *Y*) is said to be *dominant*, and its allelomorph, derived from the green-seeded race (which we shall call *y*), is said to be *recessive*. It makes no difference which race is used as mother (ovule parent) and which as father (pollen parent); the hybrid seeds are always yellow. This seed color is in the cotyledons of the embryo, which is a diploid organism containing chromosomes from both parents (p. 437), so that each

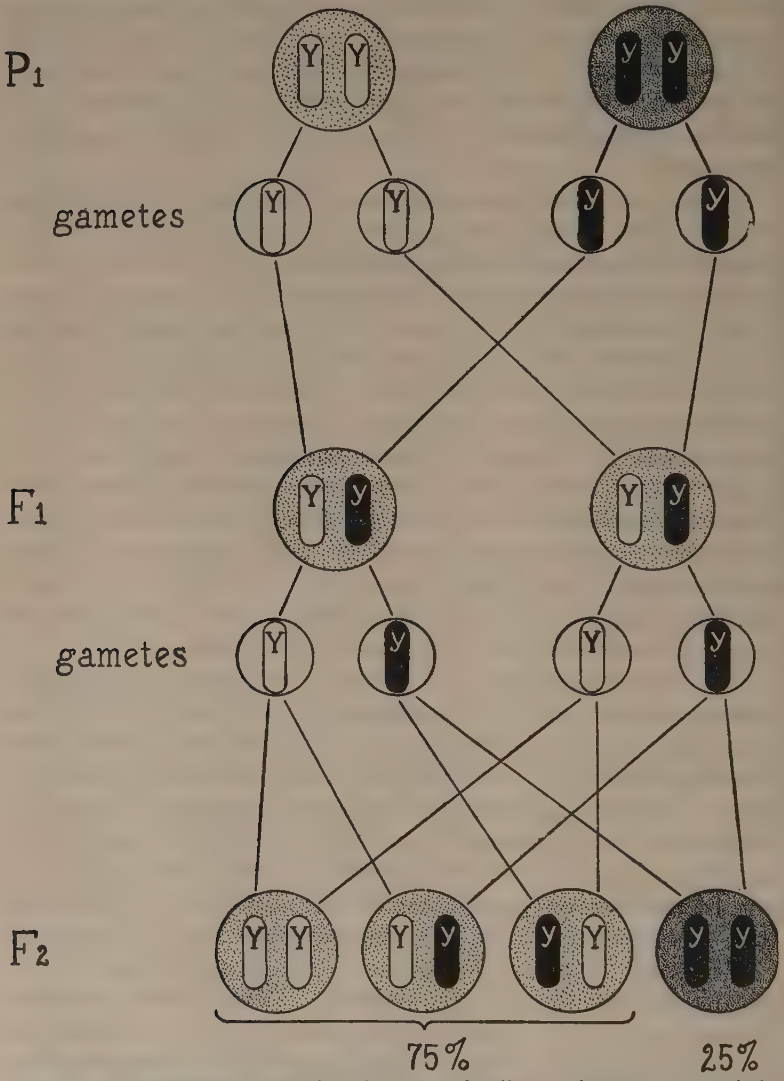

P₁
Y
Y
y
y
gametes
Y
Y
y
y
F₁
Y
y
Y
y
gametes
Y
y
Y
y
F₂
Y
Y
Y
y
y
Y
y
y
75%
25%

FIG. 154.—Diagram illustrating the cross of yellow and green peas and the inbreeding (or self-fertilization) of their offspring. The color of the heterozygous (*Yy*) peas is indistinguishable from that of the homozygous yellow (*YY*) peas.

separate seed—*i.e.*, each pea—is an *F1* individual. That these seeds are actually heterozygous, containing the genes *Y* and *y*, is shown by breeding from them. When an *F1* plant, raised from any one of the hybrid seeds, is self-pollinated it produces two kinds of *F2* seeds, yellow and green, in the ratio of 3 yellow : 1 green. The interpretation of this result may be facilitated by comparison with our previous examples: if, in the case of the Andalusian fowls, for instance, we had classified the individuals merely as "colored" and "white," all the *F1* individuals would be classed as colored, and the *F2* individuals as colored and white in the ratio of 3 colored : 1 white. The "colored" *F2* individuals, however, do not actually constitute a single class, but two classes: homozygotes (black) and heterozygotes (blue), the latter being twice as numerous as the former. This comparison suggests that our *F2* peas really consist of 25% homozygous yellow (*YY*), 50% heterozygous (*Yy*), and 25% homozygous green (*yy*), but the heterozygous peas are, just as in the *F1* generation, yellow in color and therefore indistinguishable *in somatic appearance* from the homozygous yellow class. This interpretation may be represented diagrammatically thus:

F1 eggs	*Y*	*y*	
F1 sperms *Y*	*YY* yellow	*Yy* yellow	*F2* zygotes
y	*Yy* yellow	*yy* green	

This interpretation is confirmed by breeding from the *F2* peas. All the *F2* plants from green seeds (*yy*) give, when self-pollinated, only green *F3* peas. One-third of the *F2* plants from yellow seeds give, when self-pollinated, only yellow *F3* peas; these are the homozygous yellow (*YY*) plants, constituting 25% of the total *F2* plants. The other two-thirds of the *F2* plants from yellow seeds give, when self-pollinated, both yellow and green peas, in the ratio of 3 yellow : 1 green, just as the *F1* plants did; these are the heterozygous (*Yy*) plants, constituting 50% of the total *F2* plants. The same results are repeated in subsequent generations: the homozygous plants when self-pollinated give only offspring like themselves; the heterozygous plants when self-pollinated give both yellow and green offspring in the ratio of 3 : 1.

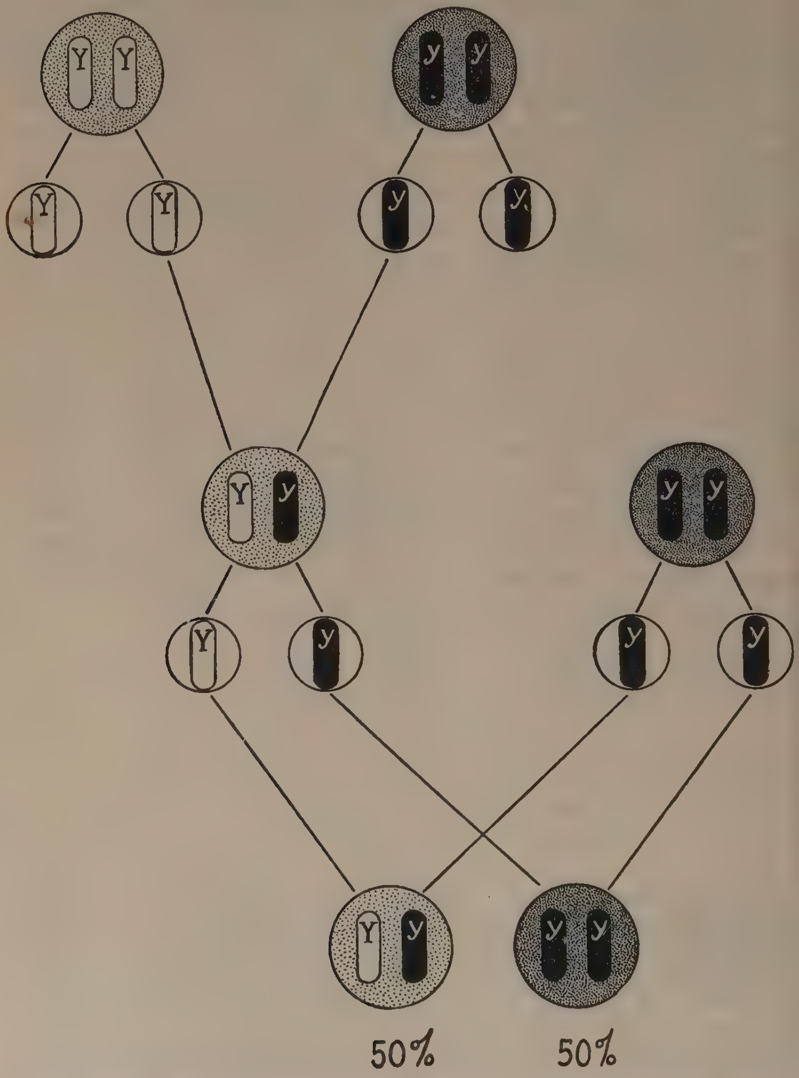


FIG. 155.—Heterozygous yellow pea, from cross of yellow and green, back-crossed to homozygous green.

This interpretation can be tested in another way—by crossing one of the F_1 plants to a plant of the green-seeded race, *i.e.*, a homozygous green (*yy*) plant. This type of cross—a heterozygote to the homozygous recessive—is called a *back-cross*. This cross gives yellow and green offspring in the ratio of 1 yellow : 1 green. Further tests of these offspring show that all the yellow ones are heterozygous, while the green ones are homozygous. This is what we should expect if the F_1 plant is heterozygous, containing the genes *Y* and *y;* by segregation, half its gametes contain the gene *Y*, the other half *y*. The homozygous green plant contains the genes *yy*, and all its gametes contain *y*. Half the offspring of the back-cross are therefore *Yy*, heterozygous yellow; the other half are *yy*, homozygous green.

The only difference between this example and the previous ones is that the combination *Yy* produces the same visible effect—yellow color of the cotyledons—as the combination *YY;* or, to put it in another way, in the presence of the gene *Y*, the gene *y* produces no visible effect. This phenomenon of *dominance* evidently concerns the developmental effects of the genes, not their hereditary transmission. It is of no significance so far as heredity is concerned, merely obscuring the results to a certain extent: in such cases we cannot judge the genetic constitution of an individual by its appearance, but only by breeding from it. These cases of dominance furnish very striking confirmation of the Law of Segregation and the purity of the genes; for the recessive gene in the heterozygote, though its visible effects are suppressed by its dominant allelomorph, is itself entirely unchanged and segregates at the maturation of the germ cells exactly as it entered the zygote.

Every intermediate condition may be found, in various pairs of allelomorphs, between complete dominance, as in the last example, and entire absence of dominance, as in our previous examples; *i.e.*, the heterozygote may resemble one homozygote more than the other to various degrees in different cases. Whenever the heterozygous class can not be sharply separated, by somatic appearance, from one of the homozygous classes, we call the allelomorph derived from this homozygote dominant. Dominance, in this sense, is the rule rather than the exception.

It is convenient to designate allelomorphic genes by the same letter, using a capital for one allelomorph and a small letter for the other, as in the examples used above. When one gene is dominant, the capital letter is used for the dominant gene, the small letter for the recessive; otherwise the choice is purely arbitrary. The letter used may be the initial letter of a word describing the somatic character determined by one of the allelomorphs (either one), as in the examples above, or may be arbitrarily selected from the alphabet. There are various other methods of designating genes, but this system will be used throughout this book. We may also, to save words, speak of a "gene for yellow" or a "yellow gene," meaning a gene which determines a yellow color of some part of the organism. Two other terms which are very useful in discussions of heredity are *genotype*, meaning organisms of a particular genetic constitution, and *phenotype*, meaning organisms with particular visible characteristics; *e.g.*, in the *F2* generation of the pea cross described above we had three genotypes, *YY*, *Yy*, and *yy*, but only two phenotypes, yellow and green.

Independent assortment.—All the experiments described above are one-factor crosses, *i.e.*, crosses involving a difference in only one pair of allelomorphic genes in each case. We have now to see what happens in crosses between races having two (or more) hereditary differences, *i.e.*, differences in two (or more) pairs of allelomorphic genes. As an example of a *two-factor cross* we may cross two races of peas, one having *yellow round* seeds, the other *green wrinkled* seeds. The color and shape are both characters of the cotyledons of the embryo. The *F1* peas, produced by crossing these races, are all *yellow* and *round; i.e.*, yellow is dominant to green, as we have previously seen, and round is dominant to wrinkled. When any one of the *F1* plants raised from these seeds is self-pollinated, it produces *four* kinds of *F2* peas: yellow round, green wrinkled, yellow wrinkled, and green round; *i.e.*, not only the two original (*P1*) combinations, but also the two possible *recombinations* of the characters involved. If we classify these *F2* peas for color alone, we find 3 yellow : 1 green, just as in the one-factor cross. Also, if we classify the same peas for shape alone, we find 3 round : 1 wrinkled, as we should expect since we have seen that round is dominant to wrinkled. Furthermore, if we classify the yellow *F2* peas alone for shape, we find 3 round : 1 wrinkled among them; and we also find the same ratio of 3 round : 1 wrinkled among the green *F2* peas. Similarly, if we classify these peas first for shape and then each of these two classes for color, we find 3 yellow : 1 green among the round peas, and 3 yellow : 1 green among the wrinkled peas. In other words, the distribution of the two colors among the *F2* peas is entirely *independent* of the distribution of the two shapes among these same peas. The resultant numbers of the four classes of *F2* peas are in the proportions of 9 yellow round : 3 yellow wrinkled : 3 green round : 1 green wrinkled. These proportions result simply from the superposition of one 3 : 1 ratio on the other; this may be made clearer by the following diagram:

$$\begin{array}{lccccccc}
 & \text{yellow} & & \text{green} & & \text{total} & & \\
\text{round}\ldots\ldots\ldots\ldots & 9 & + & 3 & = & 12 & & \\
 & & & & & \overline{} & = & 3:1 \\
\text{wrinkled}\ldots\ldots\ldots & \underline{3} & + & \underline{1} & = & 4 & & \\
\text{total}\ldots\ldots\ldots\ldots & 12 & : & 4 & = & 3:1 & &
\end{array}$$

If instead of using for the original cross yellow round and green wrinkled parents, as we did above, we cross instead two plants having the opposite combinations of these same characters—a plant from a race with *yellow wrinkled* seeds and one from a race with *green round* seeds—we get exactly the same results: all the *F1* peas are yellow and round, and their *F2* offspring are in the proportions of 9 yellow round : 3 yellow wrinkled : 3 green round : 1 green wrinkled. The results, therefore, are quite independent of which particular combinations of these characters existed in the *P1* plants: the visible characteristics of the *F1* peas and the proportions of the four classes in *F2* are due solely to the facts that yellow is dominant to green and round is dominant to wrinkled.

The results of these experiments indicate that the inheritance of the color factors is entirely independent of the inheritance of the shape factors. Similar results are obtained in many other two-factor crosses—*i.e.*, crosses involving two hereditary differences—in animals as well as in plants (in dioecious organisms, where self-fertilization is impossible, the *F1* are inbred, *i.e.*, mated brother to sister;

this makes no difference in the results). These results can all be explained by the hypothesis that the two characters involved in the experiment—*e.g.*, the color and the shape of the peas in the example used above—are determined by two *different pairs of allelomorphic genes* located in two *different pairs of homologous chromosomes.* The yellow round race, for instance, has the gene *Y* in each member of one pair of chromosomes, and the gene *R* in each member of another pair of chromosomes. Each of its gametes contains one member of each of these pairs, and therefore every gamete contains the genes *Y* and *R*, in different chromosomes. Similarly, every gamete of the green wrinkled race contains *y* and *r*. The *F1* zygote therefore receives from one parent chromosomes containing the genes *Y* and *R*, and from the other parent chromosomes containing the genes *y* and *r*. Each of these chromosomes is, of course, distributed to every diploid cell of the *F1* plant by mitosis; this plant is therefore heterozygous for both these pairs of allelomorphs, but shows phenotypically only the effects of the dominant genes *Y* and *R*. The two chromosomes containing *Y* and *y* are homologous chromosomes, and those containing *R* and *r* are another pair of homologous chromosomes. We may, for convenience, designate each of these chromosomes by the same letter as the gene it contains. At the maturation of the germ cells of this *F1* plant, each germ cell receives one member of each pair of homologous chromosomes; *i.e.*, either *Y* or *y*, *and* either *R* or *r*. But there are two ways in which these two pairs of chromosomes may be distributed at the reduction division; namely:

$$\begin{array}{c|c} Y & y \\ R & r \end{array} \quad \text{or} \quad \begin{array}{c|c} Y & y \\ r & R \end{array}$$

In the first case, the gametes of the *F1* will contain the same *combinations* of chromosomes and of genes which this plant received from its two parents, *YR* and *yr;* in the second case, these gametes will contain the new combinations *Yr* and *yR*. Which of these two distributions actually occurs in any particular case depends simply on how each pair of homologous chromosomes happens to be oriented with reference to the two poles of the spindle at the reduction division, and this is *purely a matter of chance.* The orientation of one pair has no influence on that of any other pair, and therefore the distribution of the two members of one pair is entirely *independent* of the distribution of other pairs. For the two pairs of chromosomes we are considering, therefore, the two methods of distribution shown above are equally likely to occur, and do occur, on the average, with equal frequency. Thus each of our *F1* plants produces four classes of gametes, containing the genes *YR*, *yr*, *Yr*, and *yR* respectively, in equal numbers. This is true of both the male and the female gametes.

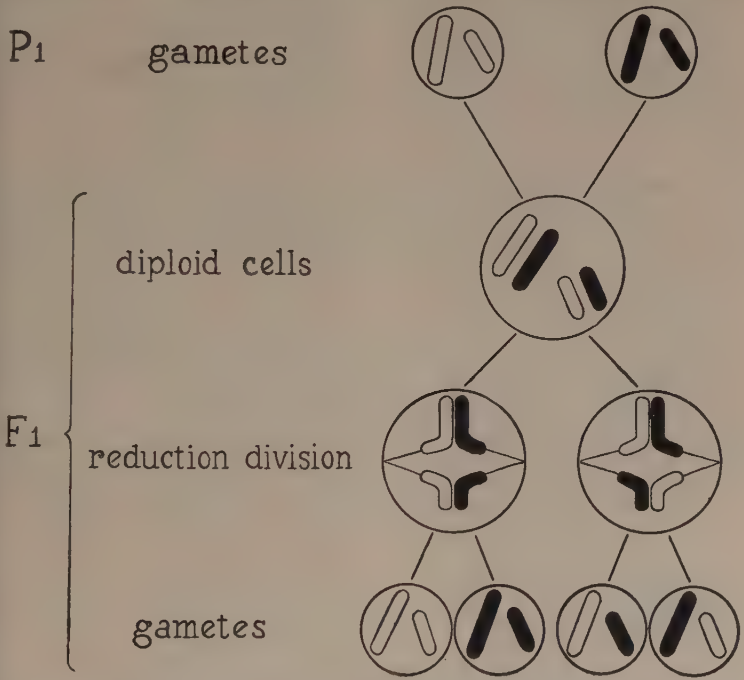


FIG. 156.—Diagram illustrating the independent assortment of two pairs of chromosomes, forming four classes of gametes in equal numbers. Homologous chromosomes of the same size; chromosomes from one parent represented as white, those from the other parent as black.

An *F1* plant produced by crossing a plant of the yellow wrinkled race, each of whose gametes contains *Y* and *r*, to one of the green round race, each of whose gametes contains *y* and *R*, has exactly the same genetic constitution as the *F1* plant discussed above; namely, the genes *Y* and *y* in one pair of homologous chromosomes, and the genes *R* and *r* in another pair. The distribution of these chromosomes at the reduction divisions is just the same as in the previous case, for this distribution is in no way affected by the respective origins of the two chromosomes of each pair. This plant, therefore, also forms the four classes of gametes, containing the genes *YR*, *yr*, *Yr*, and *yR* respectively, in equal numbers. In other words, it makes no difference which combinations of these genes are derived from each parent; the individual heterozygous for the two pairs of genes produces the four classes of gametes, representing the four possible combinations of one allelomorph of each pair, in equal numbers, the two new combinations occurring just as frequently as the combinations originally derived from its parents.

When any one of these *F1* plants is self-pollinated (or when the *F1* plants are inbred) any sperm is equally likely to fertilize any egg-cell; *i.e.*, one-fourth of the egg-cells of any particular genetic constitution will, on the average, be fertilized by each class of sperms, and the same is true of each of the other classes of egg-cells. The results of this *random fertilization* are shown in the following diagram:

F1 eggs	*YR*	*Yr*	*yR*	*yr*
F1 sperms *YR*	*YP* *YR*	*Yr* *YR*	*yR* *YR*	*yr* *YR*
Yr	*YR* *Yr*	*Yr* *Yr*	*yR* *Yr*	*yr* *Yr*
yR	*YR* *yR*	*Yr* *yR*	*yR* *yR*	*yr* *yR*
yr	*YR* *yr*	*Yr* *yr*	*yR* *yr*	*yr* *yr*

} *F2* zygotes

Since the four classes of eggs are produced in equal numbers and the four classes of sperms are also produced in equa numbers, the chance meetings of these gametes mus produce, on the average, the 16 kinds of zygotes shown in the diagram in equal numbers. Not all of these 16, however, are different, as it makes no difference whether any particular gene is received from the egg or from the sperm. These zygotes may be classified as follows:

F2 genotypes	*YR YR YR YR* *YR Yr yR yr* 1 2 2 4	*Yr Yr* *Yr yr* 1 2	*yR yR* *yR yr* 1 2	*yr* *yr* 1
F2 phenotypes	yellow round 9	yellow wrinkled 3	green round 3	green wrinkled 1

The numbers given are, of course, simply the numbers of each class to be expected among every 16 *F2* peas, *on the average*. Grouping the phenotypic classes for color and for shape separately, it will be seen that the ratio of the dominant to the recessive class in each case is 3 : 1, and also that the ratio of the two colors is the same among the peas of each shape, and conversely. These results, mathematically predicted from the hypothesis of *independent assortment* of the two pairs of allelomorphs at the maturation of the germ cells, agree exactly, it will be seen, with the results actually obtained from self-pollination of the *F1* plant.

This explanation can be further confirmed in another way—by *back-crossing* the *F1* plant to the *double recessive*, *i.e.*, the green wrinkled type. Among the offspring of this cross we find the four phenotypic classes *in equal numbers*, which is exactly what we should expect if the *F1* plant forms the four classes of gametes in equal numbers:

F1 gametes		*YR*	*Yr*	*yR*	*yr*
all gametes of the double recessive plant		*yr*	*yr*	*yr*	*yr*
offspring of the back-cross	genotypes	*YR* *yr*	*Yr* *yr*	*yR* *yr*	*yr* *yr*
	phenotypes	yellow round 1 :	yellow wrinkled 1 :	green round 1 :	green wrinkled 1

The genetic constitution of each of the genotypes in this and the preceding tables can be confirmed by breeding from them. It will be apparent from the last table that the

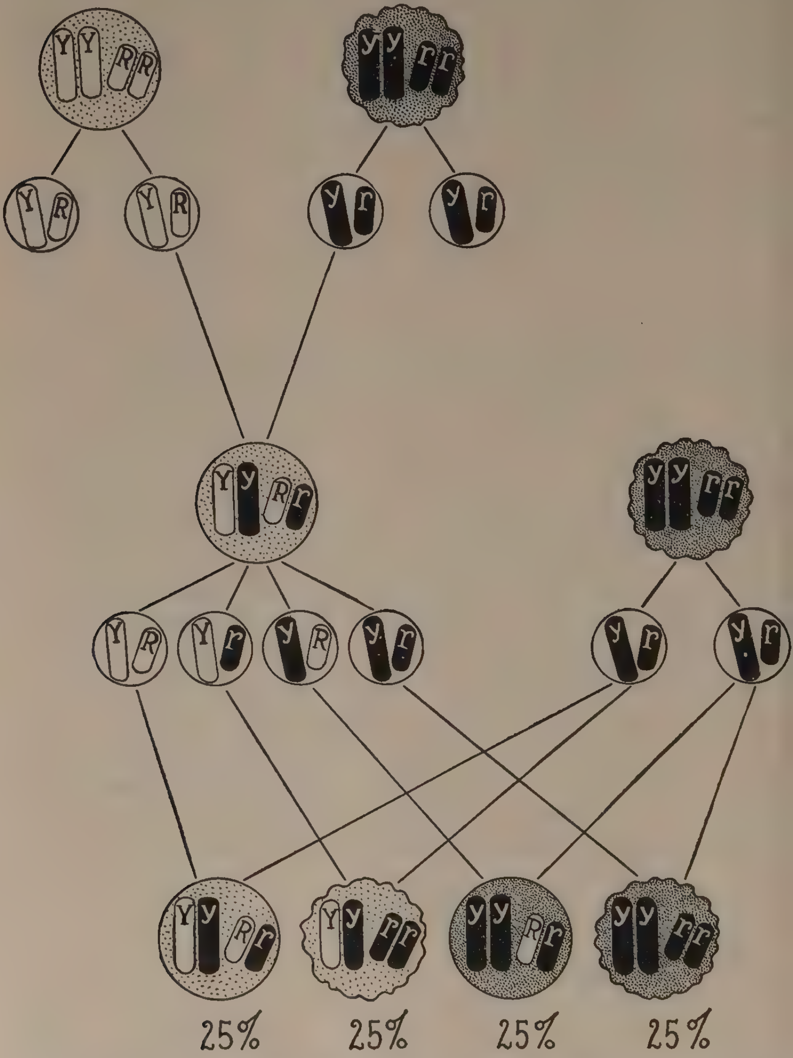

YYRR
yyrr
YR
YR
yr
yr
YyRr
yyrr
YR
Yr
yR
yr
yr
yr
YyRr
Yyrr
yyRr
yyrr
25%
25%
25%
25%

FIG. 157.—*F1* pea, from cross of yellow round and green wrinkled, back-crossed to homozygous green wrinkled.

simplest way of testing the genetic constitution of any individual is by back-crossing it to one which is homozygous for all the recessive genes, because the offspring of this back-cross correspond exactly, in their phenotypic characters, to the genetic constitution of the gametes of the individual so tested; the above table should make this clear.

Results similar in principle to those described above are obtained in crosses involving differences in three or more pairs of allelomorphs located in different pairs of chromosomes. For example, if we cross a race having the genes *A*, *B*, and *C* to one having the genes *a*, *b*, and *c*, the F_1 will produce *eight* classes of gametes, *ABC*, *ABc*, *AbC*, *Abc*, *aBC*, *aBc*, *abC*, and *abc*—all the possible combinations of one allelomorph of each pair—in equal numbers, as can be demonstrated by inbreeding the F_1 or more simply by back-crossing it to the triple recessive type. The explanation of this is the same as in the two-factor cross. The three pairs of allelomorphic genes are located in three different pairs of homologous chromosomes. These chromo-

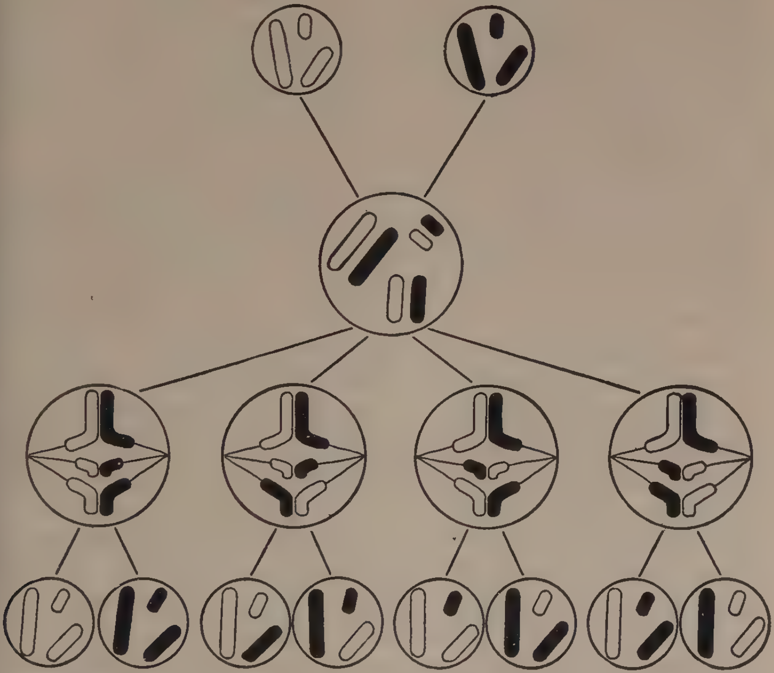


FIG. 158.—Diagram illustrating the independent assortment of three pairs of chromosomes, forming eight classes of gametes in equal numbers. Symbolism the same as in Fig. 156.

somes are distributed, at the reduction divisions in the F_1, in the four possible ways

$$\begin{array}{c|c} A & a \\ B & b \\ C & c \end{array} \qquad \begin{array}{c|c} A & a \\ B & b \\ c & C \end{array} \qquad \begin{array}{c|c} A & a \\ b & B \\ C & c \end{array} \qquad \begin{array}{c|c} A & a \\ b & B \\ c & C \end{array}$$

with equal frequency, on the average, producing the eight classes of gametes in equal numbers.

The same principles apply in cases involving differences in four or more pairs of allelomorphs, provided they are all located in different pairs of chromosomes. In all such cases, the heterozygote will produce 2^n classes of gametes *in equal numbers*, when n is the number of allelomorphic pairs for which it is heterozygous.

The results of experiments such as those described above are summarized in the Law of Independent Assortment: *the members of different pairs of allelomorphic genes are assorted independently among the germ cells at maturation.* "Independent" assortment means, of course, that all the possible combinations, consisting of one member of each pair, are formed in equal numbers. This law does *not* apply to *all* different pairs of allelomorphs, as we shall see in the following pages, but only to pairs of allelomorphs which are located in *different pairs of homologous chromosomes.*

Linkage.—From the nature of the mechanism of assortment, as explained above, it is obvious that the number of pairs of allelomorphs which are assorted independently of each other in any organism can not be greater than the number of *pairs of homologous chromosomes* in its nuclei, *i.e.*, the haploid chromosome number of that particular species. But the total number of genes—*i.e.*, of separately transmissible hereditary factors—in any organism is very much greater than the number of its chromosomes. Each chromosome, therefore, must contain many genes. Genes located in the same chromosome do not assort independently of each other, but tend to remain together in successive generations: this is called *linkage.*

Linkage is most conveniently studied in organisms with a small number of chromosomes and a large number of sharp, easily detected, hereditary differences. The most useful of all organisms for the study of heredity is the fruit-fly

Drosophila melanogaster. This small fly is very easily raised in large numbers, breeding rapidly and prolifically: each female fly lays hundreds of eggs, which develop into adult, sexually mature, flies in ten days or less. This species has only *four pairs* of chromosomes; *i.e.*, each diploid cell has eight chromosomes, each gamete only four. Several hundreds of hereditary factors have been carefully studied in this insect. These factors form four groups, all those of any one group being linked to each other in heredity but assorting independently of those in the other three groups. These four groups of hereditary factors can be identified, by several methods, with the four pairs of chromosomes, which are visibly different in size and shape (Fig. 166); *i.e.*, all the genes of any one group lie in one particular pair of homologous chromosomes. If we cross flies having two, three, or four hereditary differences determined by genes in *different* pairs of chromosomes, the results conform to the Law of Independent Assortment, exactly like those in peas described above.

As an example of a cross involving differences in two pairs of allelomorphs located in the *same* pair of chromosomes, we may cross a fly with *black* body-color and *vestigial* (*i.e.*, very short) wings to one with *gray* body-color and *long* wings (the body-color called "gray" is really a mixture of black, yellow, and brown). The *F1* flies are all *gray* with *long* wings; *i.e.*, gray is dominant to black, and long to vestigial wings. If the *F1 males* are back-crossed to black vestigial (*i.e.*, the double recessive) females, the offspring are of *two* kinds only, *black vestigial* and *gray long*, in equal numbers. If we make the original cross in the opposite way—gray vestigial × black long—the *F1* flies are again gray long, *i.e.*, show only the effects of the dominant gene of each pair. When these *F1* males are back-crossed to the double recessive (black vestigial) females, the offspring are again of two kinds in equal numbers, but these two kinds are now *gray vestigial* and *black long*. In each case the offspring of the back-cross are of *the same two kinds as the P1 flies*.

These results are easily explained on the basis that the two pairs of allelomorphic genes involved are located in the same pair of homologous chromosomes. In the first cross, the *F1* fly receives a chromosome containing the two reces-

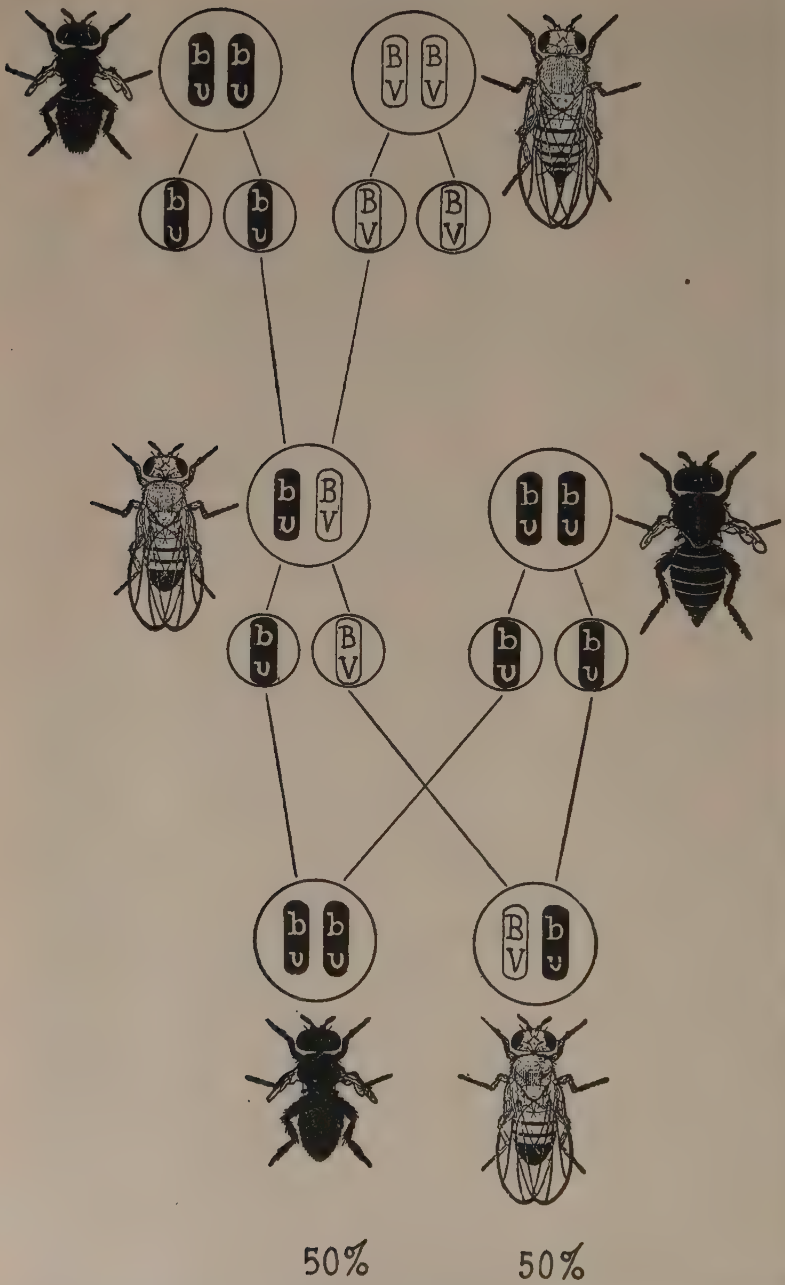


FIG. 159.—*F1* male, from cross of black vestigial and gray long, back-crossed to black vestigial female. (Adapted from Morgan.)

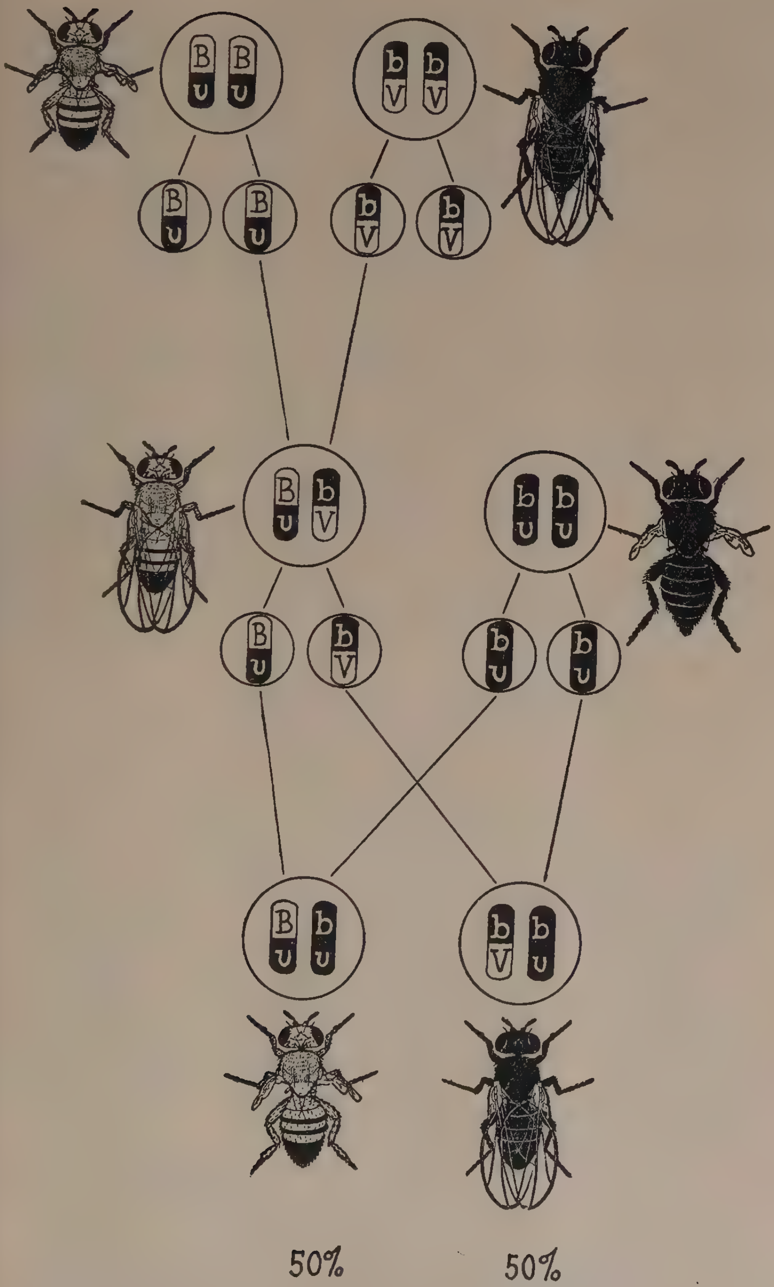

B
v
B
v
b
V
b
V
B
v
B
v
b
V
b
V
B
v
b
V
b
v
b
v
B
v
b
V
b
v
b
v
B
v
b
v
b
V
b
v
50%
50%

FIG. 160.—*F1* male, from cross of gray vestigial and black long, back-crossed to black vestigial female. (Adapted from Morgan.)

sive genes *b* and *v* from its black vestigial parent, and a homologous chromosome containing the dominant genes *B* and *V* from its gray long parent. At the reduction division, in the *F1* male, each gamete receives one of the chromosomes of this pair; therefore half the sperms contain *bv*, the other half *BV*. Back-crossed to a black vestigial female, each of whose eggs contains *bv*, half the offspring are *bvbv* (black vestigial), the other half are *BVbv* (phenotypically gray long). In the opposite cross (gray vestigial × black long) the two chromosomes in the *F1* are *Bv* and *bV* respectively, the sperms are of these two classes, and the offspring of the back-cross to black vestigial females are *Bvbv* (gray vestigial) and *bVbv* (black long). These examples show *complete linkage; i.e.*, the genes which enter the organism (the *F1* male) in the same chromosome at fertilization always remain together in the same chromosome at the maturation of its germ cells, and its gametes therefore contain only the original (parental) combinations of these genes. Any number of genes located in the same chromosome *always* maintain this relation of complete linkage in the *male* Drosophila.

It will be noted that it is carefully specified, in the above examples, that the *F1 male* is back-crossed to a double recessive female. It makes no difference which kind of fly is used as father and which as mother in the original (*P1*) cross. If, however, we back-cross the *F1 female* to a double recessive (black vestigial) male, the results are quite different from those described above. In this case, the offspring are of *four* kinds: the two original combinations and the two possible recombination classes. These four classes are, however, *not* in equal numbers, as they would be in a case of independent assortment. Taking first the cross black vestigial × gray long, and back-crossing the *F1 females* to double recessive (black vestigial) males, we find among their offspring:

black vestigial	41%	82%
gray long	41%	
gray vestigial	9%	18%
black long	9%	

Taking the opposite original cross, gray vestigial × black long, and back-crossing these *F1* females to double recessive (black vestigial) males, we find among their offspring:

gray vestigial	41%	82%
black long	41%	
black vestigial	9%	18%
gray long	9%	

In each of these cases the two *original* combinations—those derived from the *P1* flies—constitute 82% of the offspring of the back-cross, the two *new* combinations only 18%. Since all the sperms of the double recessive (black vestigial) males contain only *bv*, the proportions of the four phenotypes among the offspring of the back-cross must correspond to the proportions of the four classes of gametes—*bv*, *B V*, *Bv*, and *b V*—produced by the *F1* female in each case. The doubly heterozygous female therefore produces four classes of gametes, but the classes containing the *original combinations* of genes are, in every case, larger than the *recombination* classes. This relation of *incomplete linkage*, intermediate between complete linkage and independent assortment, is shown by all genes located in the same chromosome in the *female* Drosophila; the percentages of recombination, however, differ in different cases, as will be explained later.

The *F1* female from the cross black vestigial × gray long received from one parent a chromosome containing the genes *bv*, and from the other parent a homologous chromosome containing *B V*. Eighty-two per cent of the gametes produced by this female contain one or the other of these two chromosomes, like all the gametes of the *F1* male. The other 18% of her gametes, however, contain the new combinations *Bv* or *b V;* in these cases there has evidently been an exchange of allelomorphic genes between homologous chromosomes. In the *F1* female from the opposite cross (gray vestigial × black long), having originally the chromosomes *Bv* and *b V*, the same proportion (18%) of gametes indicate such an exchange. This exchange of material between homologous chromosomes is called *crossing-over*.

The only time in the history of the germ cells when the two homologous chromosomes come into intimate contact is at *synapsis,* which occurs in the auxocytes shortly before

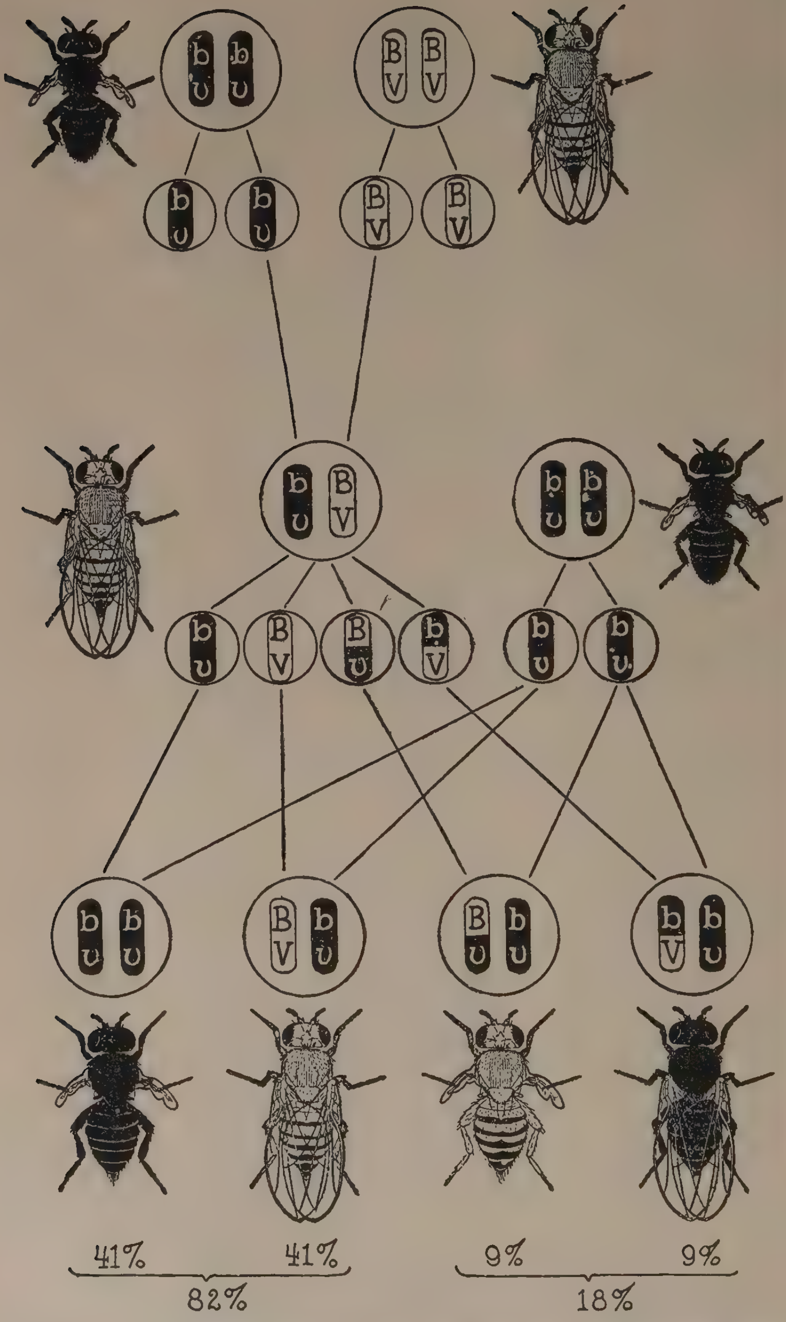

b b
v v
B B
V V
b
v
b
v
B
V
B
V
b B
v V
b b
v v
b
v
B
V
B
v
b
V
b
v
b
v
b b
v v
B b
V v
B b
v v
b b
V v
41%
41%
82%
9%
9%
18%

FIG. 161.—*F1* female, from cross of black vestigial and gray long, back-crossed to black vestigial male. (Adapted from Morgan.)

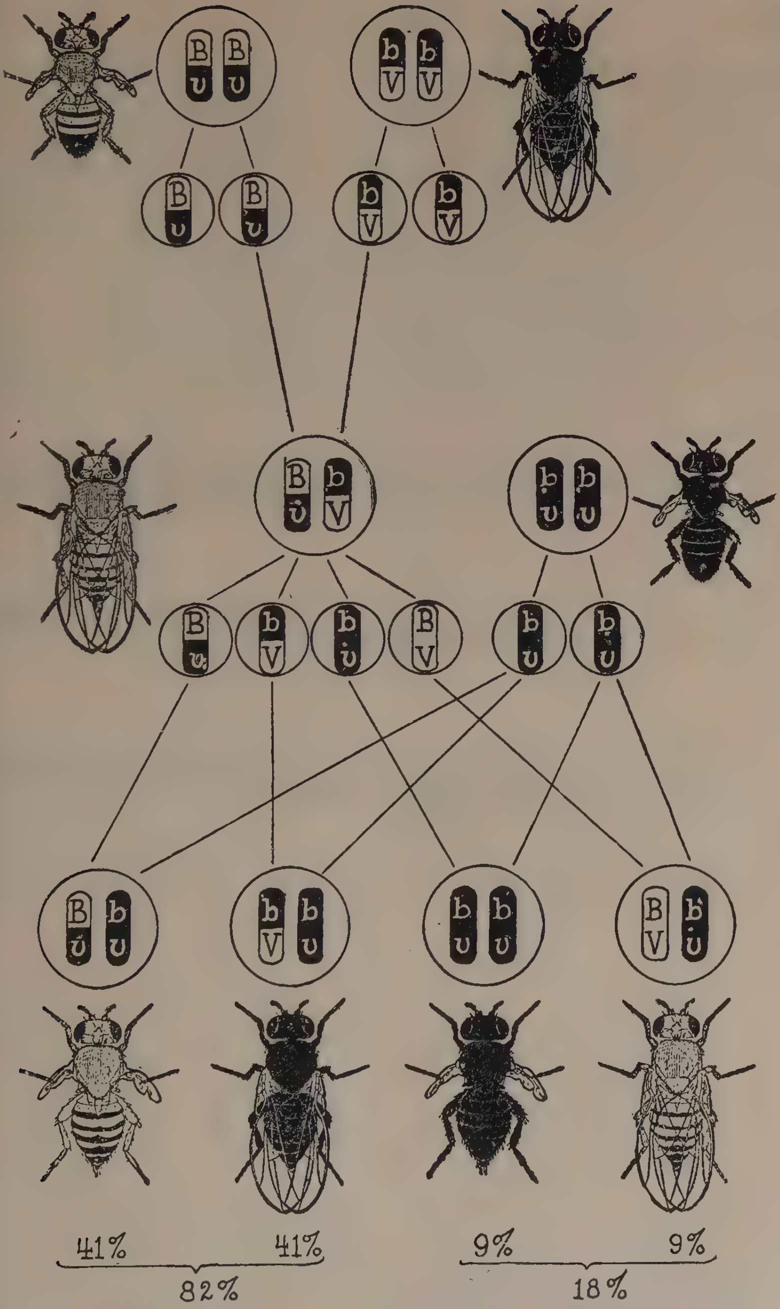

B
v
b
V
41%
41%
9%
9%
82%
18%

FIG. 162.—*F1* female, from cross of gray vestigial and black long, backcrossed to black vestigial male. (Adapted from Morgan.)

the maturation divisions (p. 411). It has been proved (by the effects of temperature and of X-rays on crossing-over) that crossing-over actually occurs at this stage. At synapsis, it will be recalled, the two homologous chromosomes of each pair come very close together, side by side, *appearing*, in many cases, to fuse completely, forming a single "thick thread" or bivalent chromosome; later each of these thick threads divides again, longitudinally, into two univalents (p. 412). Since the two homologous chromosomes (usually) *look* exactly alike, it is impossible to tell, by microscopic observation, whether the two chromosomes which separate after synapsis are individually identical with the two original members of the pair. Experiments on heredity, however, show clearly what happens during synapsis. The Law of Segregation proves that there is no actual fusion of the individual genes, since each gene always retains its own identity uncontaminated by its allelomorph or by any other gene. Crossing-over, on the other hand, shows that, in some cases at least, the two post-synaptic chromosomes are not individually identical *in whole* with the two pre-synaptic chromosomes. Crossing-over obviously involves an exchange, between the two paired chromosomes, of pieces containing allelomorphic genes. The simplest way of explaining this fact is to assume that the two chromosomes

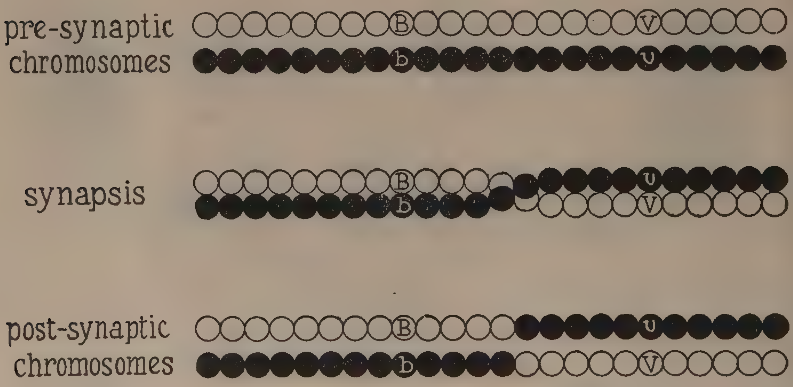


Fig. 163.—Diagram illustrating crossing-over of a pair of homologous chromosomes. If crossing-over occurs at a point which lies between the location of the genes *B* and *b* and that of the genes *V* and *v*, these genes, as the diagram shows, will occur in new combinations in the post-synaptic chromosomes.

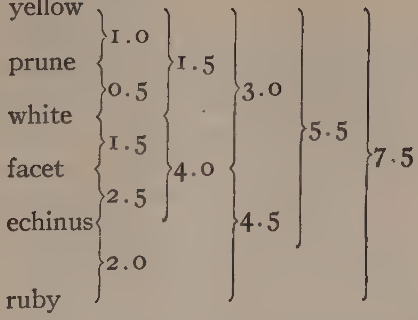
may break at a point of contact and each piece of one chromosome become attached to the other piece of its mate. When this occurs, each of the two chromosomes which separate after synapsis consists of parts of both the original chromosomes, and may therefore contain a different *combination* of genes than either of the original two; *e.g.*, if the original chromosomes contained *bv* and *B V* respectively the two cross-over chromosomes may contain *b V* and *Bv* respectively, and the gametes which receive these chromosomes at the reduction division will then contain these new combinations of genes.

From the fact that genes located in the same chromosome always show *complete* linkage in the *male* Drosophila, it is evident that, in this organism, crossing-over occurs *only in the female*. This difference between males and females, however, is not found in all organisms. In many species of animals and plants, crossing-over occurs equally in both sexes. The difference between the two sexes of Drosophila in this respect is presumably due to some difference in the process of synapsis: in the male the homologous chromosomes probably do not come into sufficiently intimate association to permit of crossing-over. The crossing-over relations among the various genes in the same pair of chromosomes are therefore always studied, in this organism, by back-crossing the heterozygous *female* to a male homozygous for all the recessive genes involved; the offspring of such a back-cross show directly, as previously explained (p. 476), the genetic constitution of the gametes of their mother.

The exchange of material between the two homologous chromosomes in crossing-over is always an exactly equal one. This is shown by both microscopic and experimental evidence. By microscopic study of the various stages of synapsis (in sections of fixed and stained auxocytes), it can be seen that the two homologous chromosomes always pair up quite precisely along their whole lengths, and are always equal in length after synapsis as well as before. When crossing-over occurs, therefore, the two chromosomes must break at exactly corresponding points and the "left" piece of one always become attached to the "right" piece of the other (Fig. 163). Experiments on heredity, such as those described above, show that each chromosome of the pair, after crossing-over, always contains one member of each pair of allelomorphic genes. These facts indicate that each gene is located at a certain definite constant position in its chromosome, and its allelomorph at an exactly corresponding position in the homologous chromosome; crossing-over therefore always involves an exchange of pieces containing allelomorphic genes. We may state this in another way: two genes located at corresponding points in homologous chromosomes behave as allelomorphs, always remaining in separate chromosomes, whether crossing-over occurs or not, and therefore always segregating into separate germ cells at the reduction division. The position of a gene in the chromosome is called its *locus*. For convenience we may designate each locus—*i.e.*, each point of the chromosome—by the name of one of the genes which may occupy this position: *e.g.*, the "black" locus, in a heterozygous fly, is occupied by the gene *b* in one chromosome and by its allelomorph *B* in the homologous chromosome; in a homozygous black fly this locus is occupied by the gene *b* in both chromosomes of this pair; in a homozygous gray fly by the gene *B* in both chromosomes.

In the experiments described above we noted that the percentage of recombination is just the same (18%) whether the two original chromosomes contained the genes *bv* and *B V* respectively or *Bv* and *b V*. The percentage of recombination is a measure of the frequency of crossing-over in the region of the chromosomes between these two loci; *i.e.*, if crossing-over occurs at some point between the black locus and the vestigial locus in 18% of all the oocytes, then the gametes produced from these particular oocytes—*i.e.*, 18% of all the gametes—will contain the new combinations of genes, while the remainder (82%) of the gametes will contain the original combinations. This does not mean that in 82% of the oocytes this pair of chromosomes has not undergone crossing-over at all, but merely that it has not occurred at any point between the black locus and the vestigial locus (unless it has occurred at two points in this interval simultaneously, which very rarely happens). The frequency of crossing-over between two loci—*i.e.*, between two particular points of the chromosome—is independent of what particular genes (*i.e.*, which of the allelomorphs) happen to occupy those loci. We can, of course, detect crossing-over directly (by means of the back-cross test) only when the organism is heterozygous for two (or more) pairs of genes located in the same pair of chromosomes; other evidence, however, demonstrates that this process goes on just the same in homozygous individuals.

When we study, by means of back-cross experiments, the linkage relations among various genes located in the same pair of chromosomes, we find that the frequency of crossing-over between any two particular loci has a definite characteristic value, but this frequency varies widely for different loci. The percentage of crossing-over between any two loci—*i.e.*, the number of cases per hundred oocytes in which crossing-over occurs between these two loci—is called the *cross-over value* of these two loci. The cross-over values of all loci in the same pair of chromosomes are found to have certain simple mathematical relations to each other. These relations may be illustrated by the cross-over values of a series of loci in one of the chromosome pairs of Drosophila; each figure is the cross-over value of the two loci indicated by the bracket (*e.g.*, yellow and prune give 1% crossing-over, yellow and white give 1.5%, yellow and ruby 7.5%, etc.):



Inspection of these figures reveals that the cross-over value of any two loci is equal to the *sum* of all the cross-over values included between these two loci; in other words, the numerical relations among the cross-over values are the same as the relations among the *distances between points in a straight line*. It is obvious that there is *only one order* in which these six loci can be arranged to give these mathematical relations; *i.e.*, if any of the loci were put at different places in the series, the additive relations of the cross-over values would not hold. Similar relations are found to hold among the cross-over values of *all* loci in each pair of chromosomes; *i.e.*, all the genes which are linked to each other can be arranged in *one, and only one, linear order* consistent with the mathematical relations among their crossing-over frequencies. The simplest, and apparently the only possible, explanation of these facts is that the genes are actually arranged in each chromosome in a definite, constant, linear order, *i.e.*, in a single line, like beads on a string. Crossing-over consists in an exchange, by homologous chromosomes, of equal and exactly corresponding pieces of these strings; this exchange does not alter the linear order of the genes, but merely substitutes, in each chromosome of the pair, one series of genes for their allelomorphs.

Another important fact about crossing-over is demonstrated by experiments in which several loci are followed simultaneously, by back-crossing female flies heterozygous for several pairs of allelomorphs, all in the same pair of chromosomes, and counting the various recombinations of these genes shown by their offspring. If the original chromosomes of the *F*1 female contain the genes

A B C D E F G H I J K L
a b c d e f g h i j k l,

we find in her gametes, as shown by the offspring of the back-cross, such recombinations as

A B C D E f g h i j k l
a b c d e F G H I J K L,

and such as *A B c d e f g h I J K L*
a b C D E F G H i j k l;

but we never find such recombinations as

A b C d E f G h I j K l
a B c D e F g H i J k L.

In other words, crossing-over always involves the exchange of relatively long pieces of the chromosomes, so that long blocks of consecutive genes always cross over together.

Crossing-over at one point of a chromosome never occurs simultaneously with crossing-over at another closely neighboring point. This relation is called *interference*, because it suggests that crossing-over at one point of a chromosome "interferes" in some way with crossing-over at a neighboring point. The most probable explanation of interference is that the two homologous chromosomes twist about each other, at synapsis, in long loops, and crossing-over can only occur at the nodes of these loops, where the two chromosomes cross. Crossing-over apparently never occurs at more than four points simultaneously in even the longest chromosomes of Drosophila.

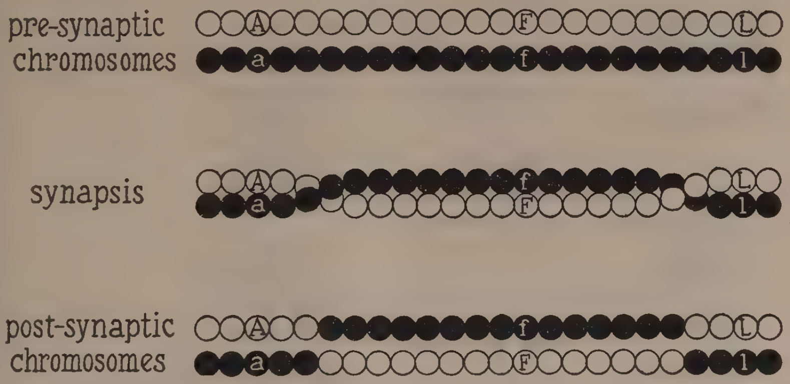


FIG. 164.—Diagram illustrating double crossing-over of a pair of homologous chromosomes. If crossing-over occurs at the points shown in the diagram, the genes *A* and *L*, and also *a* and *l*, will occur in their original combinations in the post-synaptic chromosomes; but the crossing-over will be evidenced by the interchange of the genes *F* and *f* at an intermediate locus.

When crossing-over occurs at two points in the same pair of chromosomes, *e.g.*,

A B c d e f g h I J K L
a b C D E F G H i j k l,

two genes such as *A* and *L*, which were originally in the same chromosome, are still in the same chromosome. If we were following only these two loci (*i.e.*, if the fly were homozygous for all genes at intermediate loci), we might conclude that no crossing-over had occurred between these two points, when, in fact, it had actually occurred twice in this interval. For this reason, the frequency of crossing-

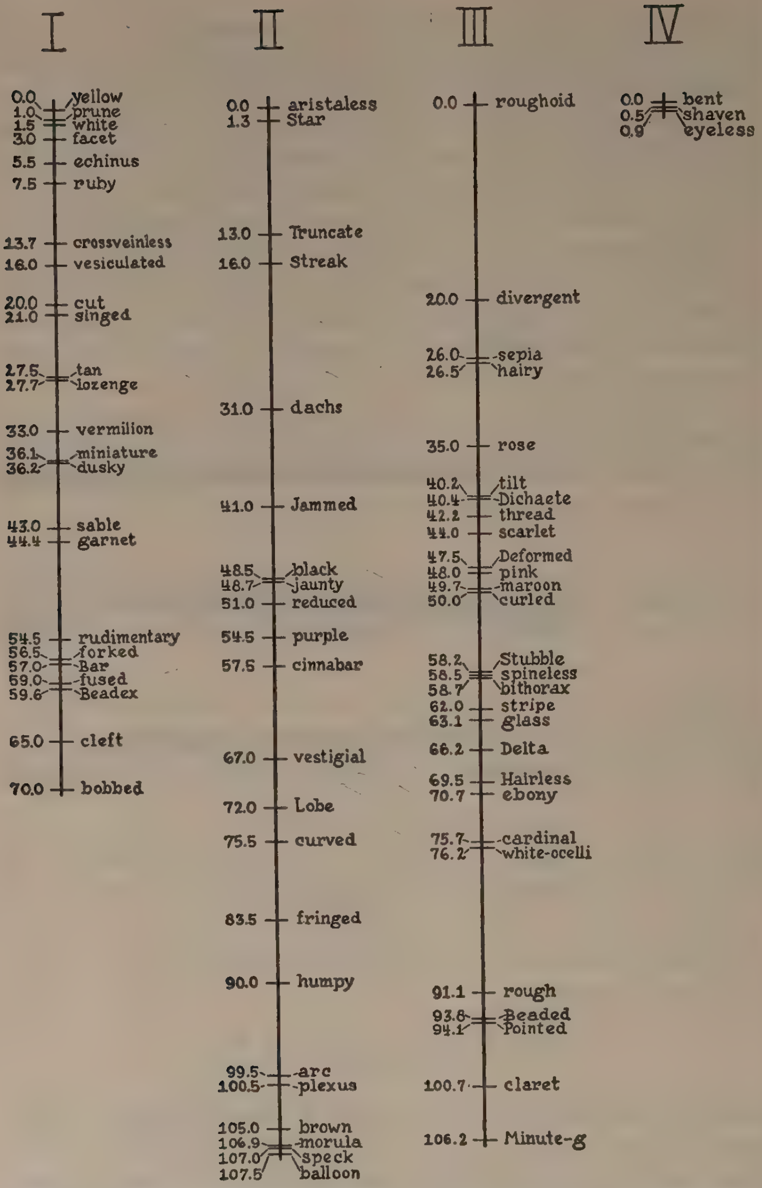

I
0.0 yellow
1.0 prune
1.5 white
3.0 facet
5.5 echinus
7.5 ruby
13.7 crossveinless
16.0 vesiculated
20.0 cut
21.0 singed
27.5 tan
27.7 lozenge
33.0 vermilion
36.1 miniature
36.2 dusky
43.0 sable
44.4 garnet
54.5 rudimentary
56.5 forked
57.0 Bar
59.0 fused
59.6 Beadex
65.0 cleft
70.0 bobbed
II
0.0 aristaless
1.3 Star
13.0 Truncate
16.0 Streak
31.0 dachs
41.0 Jammed
48.5 black
48.7 jaunty
51.0 reduced
54.5 purple
57.5 cinnabar
67.0 vestigial
72.0 Lobe
75.5 curved
83.5 fringed
90.0 humpy
99.5 arc
100.5 plexus
105.0 brown
106.9 morula
107.0 speck
107.5 balloon
III
0.0 roughoid
20.0 divergent
26.0 sepia
26.5 hairy
35.0 rose
40.2 tilt
40.4 Dichaete
42.2 thread
44.0 scarlet
47.5 Deformed
48.0 pink
49.7 maroon
50.0 curled
58.2 Stubble
58.5 spineless
58.7 bithorax
62.0 stripe
63.1 glass
66.2 Delta
69.5 Hairless
70.7 ebony
75.7 cardinal
76.2 white-ocelli
91.1 rough
93.8 Beaded
94.1 Pointed
100.7 claret
106.2 Minute-g
IV
0.0 bent
0.5 shaven
0.9 eyeless

FIG. 165.—Chromosome maps of Drosophila melanogaster, showing the loc of some of the genes which have been most accurately located. (Adapted from Morgan, Bridges, and Sturtevant.)

over between two loci which are relatively far apart in the chromosome can not be determined accurately by back-cross experiments involving only these two loci. This does not apply, however, to loci which are relatively close together in the chromosome, for, as we have seen, crossing-over never occurs twice simultaneously between such loci. The true cross-over values of all the loci in each pair of chromosomes are therefore determined by means of back-cross experiments which always involve genes whose loci are sufficiently near each other to preclude the possibility of double crossing-over between them.

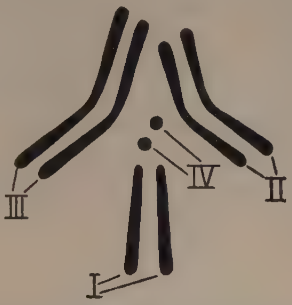


FIG. 166.—Diploid chromosome group of Drosophila melanogaster (female). The numbers *I*, *II*, *III*, *IV* designate the chromosomes which contain the genes on the correspondingly numbered maps of Fig. 165.

By combining the results of many such experiments, *chromosome maps* can be made, showing the order and cross-over values of all the loci in each pair of chromosomes, just as we did above (p. 489) for the six loci, yellow, prune, white, facet, echinus, ruby. For Drosophila melanogaster, which has been studied in this way much more extensively than any other organism, all the chromosomes have been very thoroughly mapped; those of a number of other organisms have been less completely mapped. Each chromosome map (Fig. 165) represents one pair of homologous chromosomes, the order and cross-over values of the loci being, of course, identical in the two homologous chromosomes. The loci shown on the maps are only those of genes which have been accurately located by means of back-cross experiments; there are, of course, many other genes located between these, probably several thousands in all. As a matter of convenience, all the cross-over values on each map are referred to a single locus, at one end of the chromosome, taken as 0: the true cross-over value of any two loci is simply the difference between the figures given on the map for these two loci. Since the mathematical relations among the cross-over values are, as we have seen, the same as those of distances between points on a straight line, these figures are called *map distances.*

It has been definitely proved (chiefly by means of occasional abnormalities in chromosome distribution) that the genes on the maps called II and III are in the two pairs of long V-shaped chromosomes, those on map I in the somewhat shorter straight pair, and those on map IV in the extremely small pair (Fig. 166). If we compare the total lengths, in terms of map distances, of the four maps with the actual microscopically measured lengths of the corresponding chromosomes, we find them approximately proportional:

Chromosome	*Map length*	*Actual length (at metaphase)*
I	70	1.8 μ
II	107	2.6 μ
III	106	3.2 μ
IV	1	.2 μ

This suggests that map distance is, at least approximately, a true measure of length in the chromosomes; *i.e.*, that the map distances between loci are proportional to the actual linear distances between them in the chromosomes, so that each unit on the map represents not only one unit of cross-over value (1% of crossing-over) but also a certain definite physical distance between loci. This would mean that the frequency of crossing-over between any two loci depends simply on the distance between them; *i.e.*, that crossing-over occurs as frequently, on the average, in any one region of a chromosome as in any other region of equal length. It has recently been shown, however, that this is not exactly true.

Regardless of the exactness of the proportionality between map distances and actual distances in the chromosomes, the chromosome maps, being based directly on cross-over values, enable us to predict with a considerable degree of accuracy the percentage of crossing-over between any two pairs of genes (*i.e.*, between any two loci) in the same pair of chromosomes. The total percentage of crossing-over between any two loci is equal to their map distance from each other. In an experiment in which only two loci are followed (*i.e.*, the flies are heterozygous for only two pairs of allelomorphs), the observed percentage of recombination will be equal to the true cross-over value (map distance) provided the two loci are relatively near each other (within 10 or 15 units, usually). If the two loci are farther apart, the observed percentage of recombination will be less than the true cross-over value, because of double crossing-over between them, as previously explained. For this reason, the percentage of recombination between genes in the same pair of chromosomes is always less than 50%, although the longer maps are more than a hundred units long. The percentages of recombination between these more distant loci can, however, also be accurately predicted from a knowledge of the strength of interference in different regions of the chromosomes.

Every gene in this species can be shown to occupy a definite locus in one of the four pairs of chromosomes. Genes located in different pairs of chromosomes always show independent assortment. All genes located in the same chromosome show complete linkage in the male and incomplete linkage in the female. The locus of any gene in its chromosome can be determined from its percentages of crossing-over (in the female) with any two genes in the same chromosome whose loci are known. Genes which have the same locus are allelomorphs.

The laws of linkage and crossing-over have been discovered chiefly by experiments on Drosophila melanogaster, but have been studied sufficiently in other species of animals and in plants to demonstrate that the same laws apply very generally—probably to all organisms with regular mitotic division and sexual reproduction. The phenomena of linkage are summarized in the following four laws, called Morgan's laws:

All the genes of a species form a number of linkage groups equal to the haploid chromosome number of the species, the genes in any one of these groups assorting independently of those in any other group.

All genes in the same group are linked in heredity, maintain-

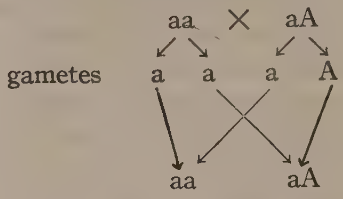
ing their original combinations at the maturation of the germ cells, either always (complete linkage) or more often than not (incomplete linkage).

All the genes in each linkage group can be arranged in a single linear order such that the frequencies of crossing-over between them have the same mathematical relations as the distances between points in a straight line.

Crossing-over at any point in the series interferes (is negatively correlated) with crossing-over at neighboring points; for short intervals this interference is complete, so that for genes relatively close together in the series the observed percentage of recombination is an accurate measure of the frequency of crossing-over between them.

These four laws, together with Mendel's two laws (Segregation and Independent Assortment), constitute an essentially complete formulation of the normal phenomena of heredity—*i.e.*, transmission of hereditary factors—in sexually reproducing organisms. Certain occasional abnormalities in the mechanism of heredity will be described in Chapter XXIV.

The inheritance of sex.—In most dioecious organisms, two kinds of individuals—males and females—are produced in equal (or very nearly equal) numbers in every generation, and each kind necessarily always mates with the other. This situation is exactly similar to what would happen if individuals heterozygous for any particular pair of allelomorphic genes were mated, in every generation, to individuals homozygous for the recessive gene of this pair; *e.g.*,



If individuals of the genetic constitution *aA* can only mate with those of the constitution *aa*, the other homozygote, *AA*, can never be produced, and the two classes *aa* and *aA* must always be produced in equal numbers. The production of males and females in equal numbers by dioecious organisms can therefore be very simply explained on the basis that one sex is heterozygous for a sex-determining gene for which the other sex is homozygous. That the sexual difference is actually inherited in this way is conclusively demonstrated by the linkage relations of the sex-determining genes to other genes located in the same pair of chromosomes. It happens, moreover, that in many kinds of organisms the two members of this particular pair of chromosomes are *visibly dissimilar* in the heterozygous sex. In Drosophila melanogaster, for instance, there are four pairs of homologous chromosomes; in three of these pairs the two homologous chromosomes are always identical in size and shape. The remaining pair consists of two

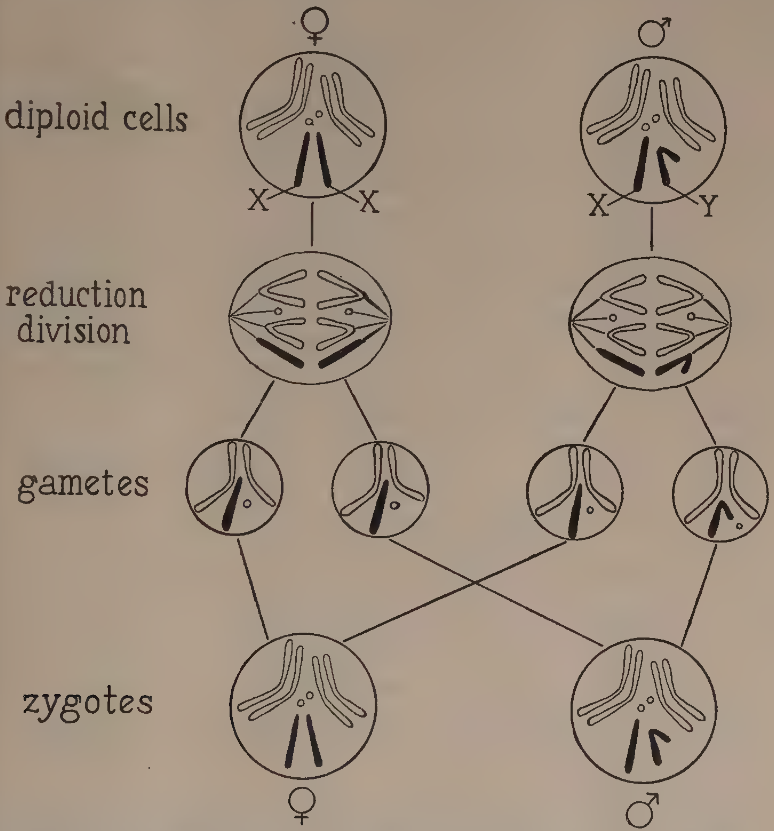
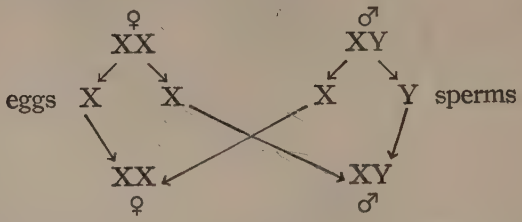


FIG. 167.—Diagram showing the distribution of the sex-chromosomes in Drosophila melanogaster. Sex-chromosomes black, autosomes white.

straight, rod-shaped chromosomes in the female; but in the male this pair consists of one straight chromosome, similar to those in the female, and one bent, J-shaped chromosome. The straight chromosomes, of which there are two in the female and one in the male, are called the *X-chromosomes;* the bent one, present only in the male, is called the *Y-chromosome;* both the *X* and the *Y* are called *sex-chromosomes.* All the other chromosomes, which are identical in the two sexes, are called *autosomes.*

Since the female contains a pair of *X*-chromosomes, each egg-cell after maturation contains one *X*-chromosome. In the male the *X* and the *Y* behave as homologous chromosomes, segregating into separate germ cells at the reduction division; half of the sperm-cells, therefore, contain the *X*-chromosome, the other half contain the *Y*-chromosome. Half of the zygotes, therefore, contain *XX* (one *X* from each gamete); the other half contain *XY* (an *X* from the egg-cell and a *Y* from the sperm). The *XX* zygotes develop as females, the *XY* zygotes as males. These facts may be represented diagrammatically thus:



The same thing will, of course, be repeated in every generation; the sexual difference is thus automatically self-perpetuating.

These microscopically visible facts would seem to suggest that each *X*-chromosome carries a recessive gene for femaleness and the *Y*-chromosome a dominant gene for maleness. This, however, is not entirely true, for the *Y*-chromosome actually has no effect at all in determining the sex. By certain rare abnormalities in the maturation divisions, individuals of Drosophila are occasionally produced which have one *X*- and no *Y*-chromosome; these individuals are always *males.* In some other animals this is the normal condition: the *X*-chromosome has no mate at all in the male; half of the sperm-cells contain the X-chromosome, the other half contain no sex-chromosome at all. Occasional individuals of Drosophila (resulting from abnormal maturation divisions) contain two Xs and a Y, or even two Xs and two Ys;

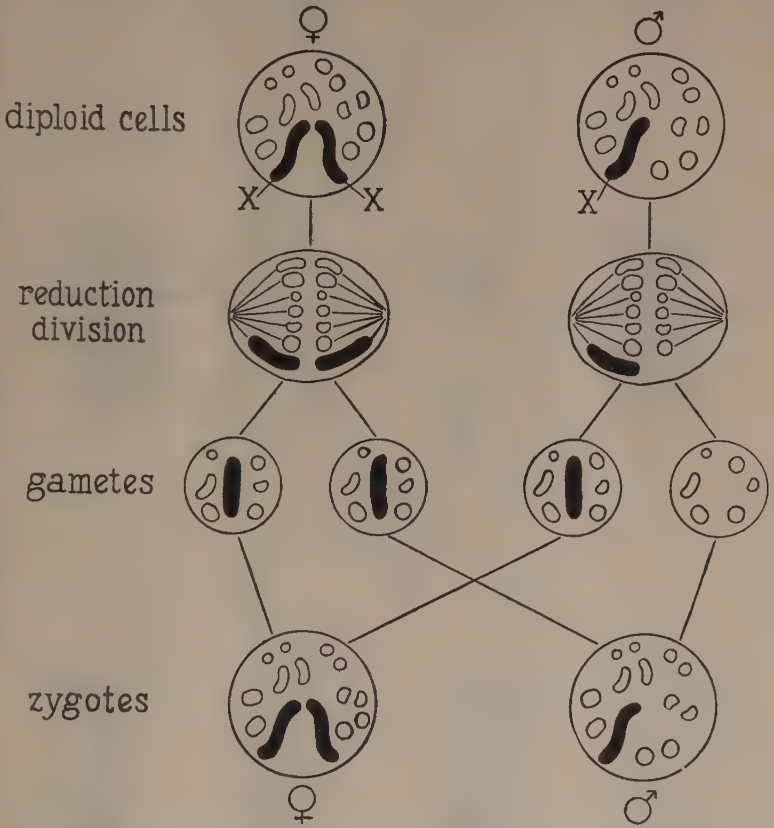


Fig. 168.—Diagram showing the distribution of the sex-chromosomes in Protenor, a bug which has no Y-chromosome. Sex-chromosomes black, autosomes white.

such individuals are *females*. The primary difference between females and males, which determines the differences in their reproductive organs and other sexual characters, is therefore simply that the female contains twice as much of some factor carried by the X-chromosomes. We may think of this sex-determining factor as a gene for "femaleness" for which the female is homozygous, while the male is hetero-

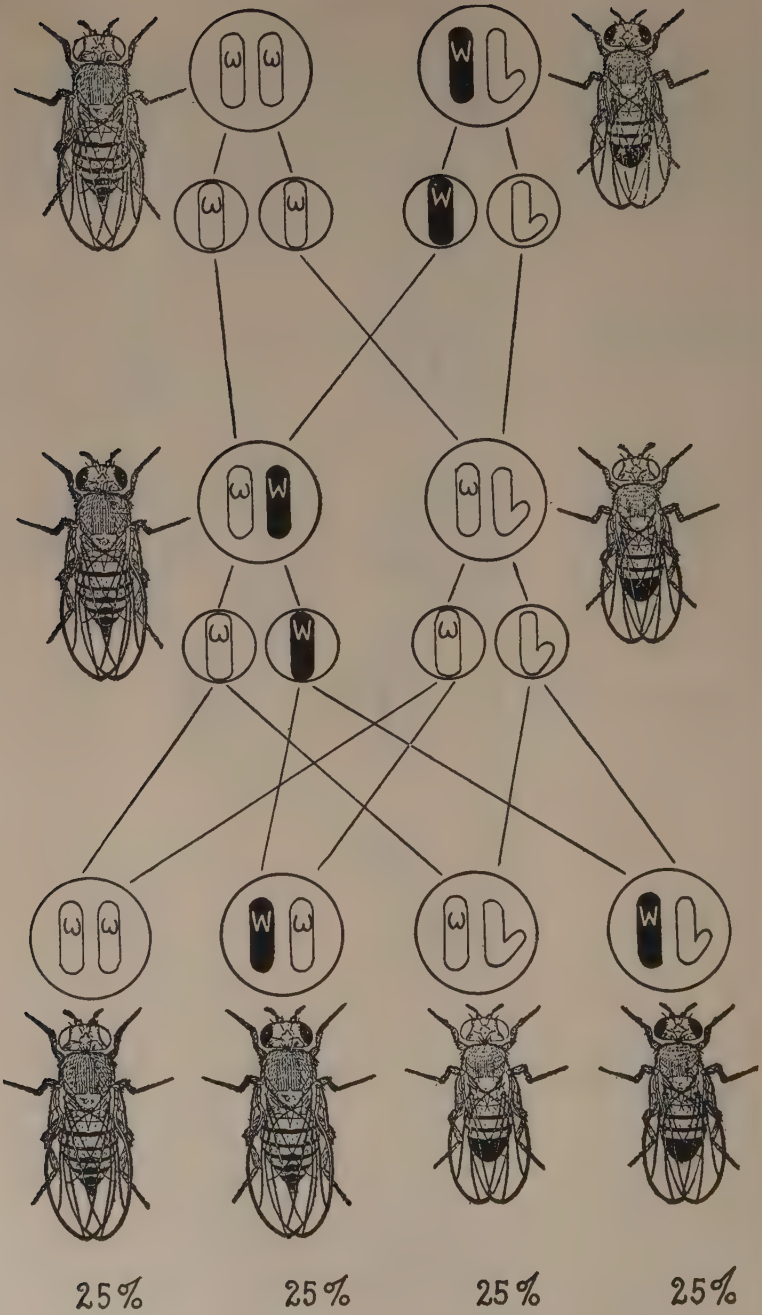

ω ω
W L
ω
ω
W
L
ω W
ω L
ω
W
ω
L
ω ω
W ω
ω L
W L
25%
25%
25%
25%

Fig. 169.—Cross of white-eyed female and red-eyed male; *F1* inbred. (Adapted from Morgan.)

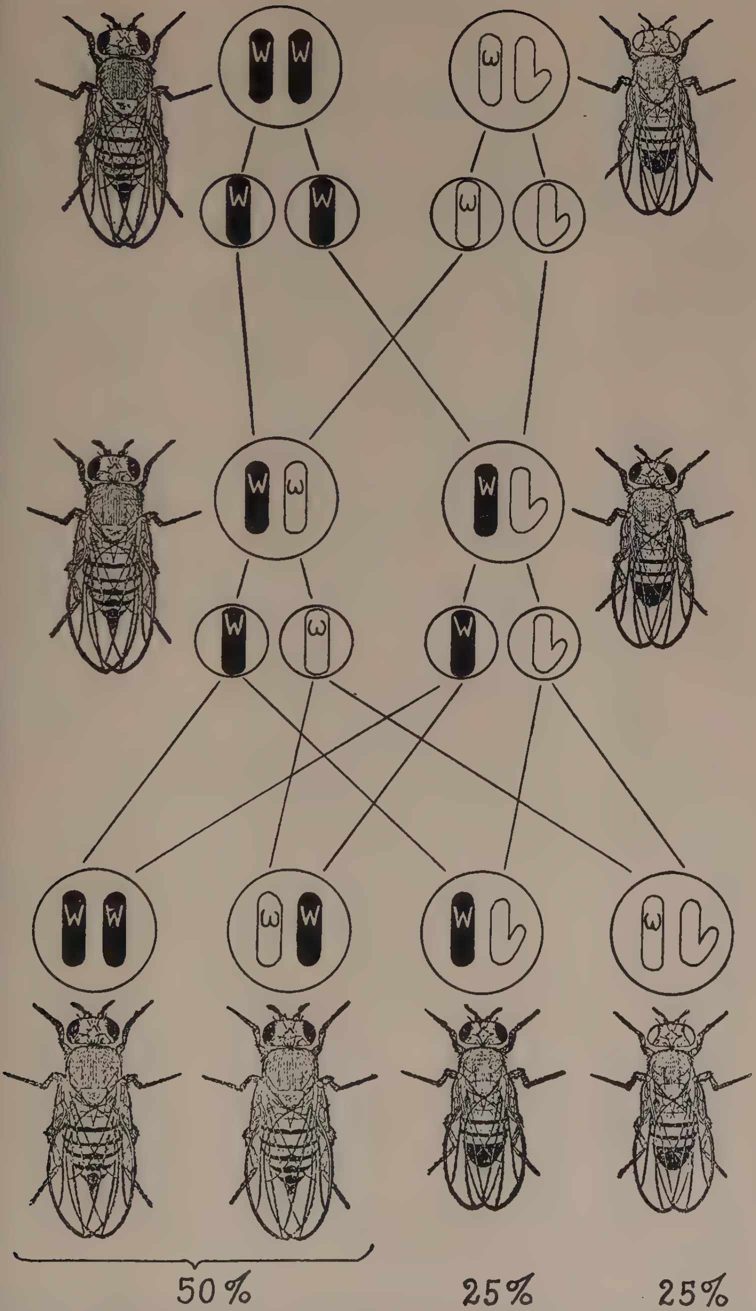

W
W
ω
W
W
ω
W
ω
W
W
ω
W
W
W
ω
W
W
ω
50%
25%
25%

FIG. 170.—Cross of red-eyed female and white-eyed male; *F1* inbred. (Adapted from Morgan.)

zygous in the sense that he contains this gene in only one chromosome and consequently transmits it to only half of his gametes. Other evidence (p. 562) shows that the autosomes contain genes for "maleness," but since both sexes are homozygous for these, the *difference* between males and females is determined by the number of *X*-chromosomes they contain.

From what we have previously learned of the mechanism of linkage, it is obvious that all other genes located in the *X*-chromosomes must be linked to the sex-determining factor; these genes are called *sex-linked*. All the genes of linkage group I in Drosophila are sex-linked, showing that these genes are located in the *X*-chromosomes. The peculiar features of inheritance of sex-linked genes may be illustrated by the cross of red-eyed flies to white-eyed flies, the genes responsible for this difference being in the sex-linked group. If a *white-eyed female* be crossed to a *red-eyed male*, all their *daughters* have *red* eyes and all their *sons* have *white* eyes. When these *F1 females* are mated to white-eyed males, half of their offspring (*F2*), regardless of sex, have red and half have white eyes: this indicates that *F1* females are heterozygous (*Ww*), as we should expect, and that red is dominant to white. If these *F1* females are mated to their brothers, the *F1 males*, the results are just the same as when they are mated to males from the original white-eyed race. Also, the *F1* males back-crossed to white-eyed females give only white-eyed offspring. These facts indicate that the genetic constitution of the *F1* males is the same as that of males from the original white-eyed race; *i.e.*, these males have not inherited the gene *W* (the gene for red eyes) from their red-eyed father.

When we make the original cross the other way—*red-eyed female* by *white-eyed male*—*all* the *F1* flies have *red* eyes. These *F1 females* are found to be heterozygous (*Ww*), just as in the previous cross. The *F1 males* in this case give results, in all crosses, just like males from the original red-eyed race; *i.e.*, these males give no indication of having inherited the gene *w* (the gene for white eyes) from their white-eyed father.

All crosses involving sex-linked genes (genes in linkage group I) in Drosophila give results similar to these: the daughters receive one allelomorph of each pair from each parent, just as in the case of non-sex-linked genes; but the *sons receive no sex-linked genes from their father*. This obviously means that the *Y*-chromosome contains *no genes at all*—it is merely a "dummy" chromosome. The male, therefore, inherits sex-linked genes from his mother only, and transmits them to his daughters only. With this exception the inheritance of sex-linked genes conforms to all the same laws as that of other genes.

All sex-linked genes are, of course, linked to each other, since they are all in the same pair of chromosomes, and show the usual relations of complete linkage in the male Drosophila and incomplete linkage (crossing-over) in the female. The locations of these genes in the *X*-chromosomes can be determined in the usual way, by back-crossing heterozygous females; but the location of the sex-determining gene itself can not be determined in this way, because all females are homozygous for this gene, and there is no crossing-over in the male. For this reason we have as yet no idea as to where this gene is located in the *X*-chromosome. In some other animals, in which crossing-over occurs in both sexes. there is evidence of crossing-over between the *X* and the *Y*, but these cases have not yet been studied sufficiently to locate the sex-determining gene very precisely.

The same type of sex-determining mechanism as in Drosophila—*i.e.*, the males heterozygous for a sex-factor for which the females are homozygous—has been found in most animals in which the question has been studied (many arthropods, vertebrates, echinoderms, nematodes, etc.) and also in some dioecious seed-plants (*i.e.*, plants in which the sporophyte is dioecious). In many species there is no *Y*-chromosome, the female having two *X*s and the male a single unpaired *X* which is distributed to half the sperm-cells at the reduction division. In other species there is normally a *Y*-chromosome, visibly distinguishable from the *X*, in the male; but in some of these species the *Y* may be absent in some males. In some species there is no visible difference between the *X* and the *Y*, but the inheritance of sex-linked genes shows that the mechanism of sex-determination is the same as in the other cases. In all these organisms the mode of inheritance of sex-linked genes is the same as that described above for Drosophila. A number of sex-linked genes, inherited in this way, are known in man, where there is a visibly dissimilar XY pair in the male (the Y may perhaps be absent in some males). In some species there are also genes in the Y-chromosome, which are transmitted through the male line only.

In organisms with this type of sex-determining mechanism, the sex of the zygote is determined by the genetic constitution of the sperm-cell; *i.e.*, every egg-cell contains one X, but the sperms are of two kinds, *female-producing* (containing an X-chromosome) and *male-producing* (containing a Y or no sex-chromosome). These two classes of sperms are produced in equal numbers, by the mechanism of segregation, and the two kinds of zygotes—male and female—are therefore usually produced in equal numbers. Inequalities in the numbers of males and females may occur in some cases because of unequal viability or activity of the two classes of sperms or unequal viability of the male and the female zygotes.

In a few groups of animals (moths, birds, some species of fishes) the mechanism of sex-determination is exactly opposite to the usual type: the females are heterozygous for a sex-factor for which the males are homozygous. In these animals the two sex-chromosomes are alike in the males; in the females they may be visibly dissimilar or there may be only one. In these cases the sex-determining factor must be a gene for "maleness" for which the males are homozygous and the females heterozygous. In organisms with this type of sex-determining mechanism, the sperm-cells are all of one kind while the egg-cells are of two classes, female-producing and male-producing. In these animals the mode of inheritance of sex-linked genes is also exactly opposite to that in Drosophila, as would be expected; *i.e.*, the males inherit sex-linked genes from both parents and transmit them to all their offspring, but the females inherit these genes from their fathers only and transmit them to their sons only.

Several types of sex-determining mechanisms have been found in animals which reproduce parthenogenetically (p. 415). In all cases of natural haploid parthenogenesis the haploid individuals are males, while the diploid individuals developing from fertilized eggs are females. In these animals (*e.g.*, bees, wasps, etc.) all genes are inherited in the same way as the sex-linked genes in Drosophila; *i.e.*, the males inherit only from their mothers (since they have no fathers), while the females inherit equally from both parents. In the rotifers, which reproduce by both diploid and haploid parthenogenesis as well as sexually, all diploid individuals, whether parthenogenetically or sexually produced, are females, while the haploid individuals are males. Some animals produce both females and males by *diploid* parthenogenesis. In diploid parthenogenesis, it will be recalled, there is a single polar body formed by an ordinary (equational) mitotic division. In cases where both sexes are produced in this way (*e.g.*, in aphids), it has been found that in *some* of the parthenogenetic eggs one chromosome is lost at this division, by lagging behind on the spindle and failing to enter the egg-nucleus. These eggs develop into males, while eggs with the complete diploid number of chromosomes develop into females. The chromosome which is lost from the male-producing eggs can be identified by its size and shape as being always one of a particular pair; *i.e.*, it is one of the X-chromosomes. The female therefore has two X-chromosomes and the male only one. At the reduction division in the male only half of the sperm-cells receive an X-chromosome; but those of the no-X class degenerate, only the X-bearing sperms being functional: all the sexually produced individuals, therefore, are females.

It has been mentioned above that plants in which the sporophyte is dioecious have, in those cases which have been studied, the same mechanism of sex-determination as most dioecious animals (female XX, male XY). A quite different type of sex-determining mechanism is found in some of the bryophytes in which the gametophyte is dioecious (p. 427). In the diploid nuclei of the sporophyte the two chromosomes of one pair are visibly dissimilar; these two chromosomes are called X and Y. At the reduction division half of the spores receive the X-chromosome, the other half the Y. The X-bearing spores develop into female gametophytes, the Y-bearing spores into males. All the nuclei of the female gametophyte contain X only, those of the male Y only, these nuclei being, of course, haploid (p. 427). As the gametophyte produces the gametes by ordinary mitotic divisions, all the eggs contain *X*, all the sperms *Y*. Every zygote, therefore, and every diploid cell of the sporophyte contain both *X* and *Y*, but here they have no sex-determining function, as the sporophyte has no sex at all.

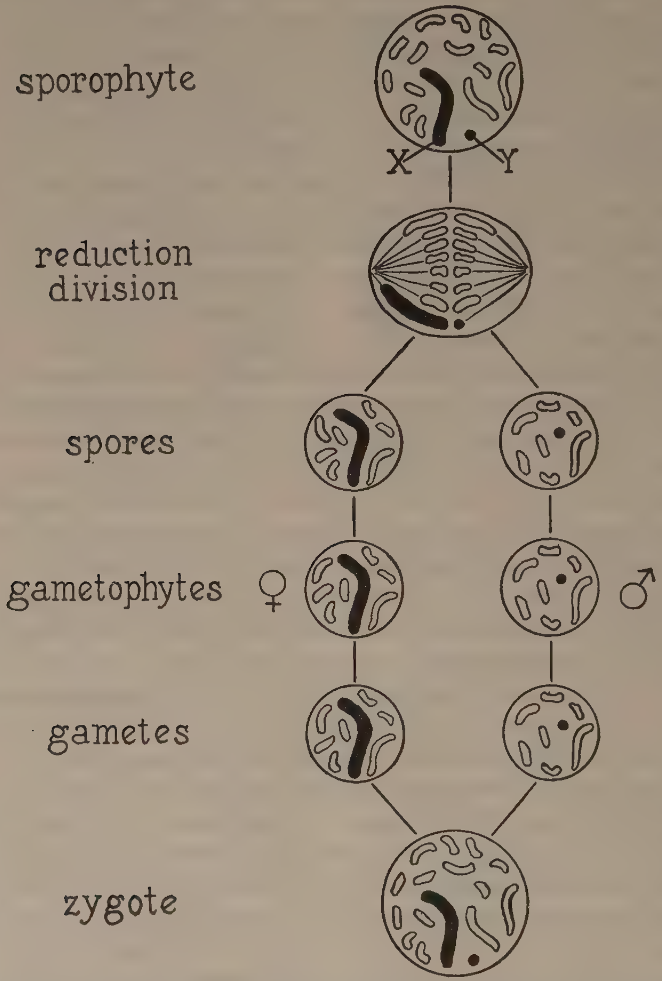

sporophyte
X
Y
reduction division
spores
gametophytes
♀
♂
gametes
zygote

Fig. 171.—Diagram showing the distribution of the sex-chromosomes in Sphaerocarpos, a dioecious bryophyte. Sex-chromosomes black, autosomes white.

In all these various types of sex-determining mechanisms, the essential point is that the *differences* between the two kinds of *individuals*—males and females—are determined by differences in their genetic constitution, which are frequently, though not necessarily, accompanied by microscopically visible differences in their chromosomes. In monoecious (and also in asexual) organisms, there are, of course, no such genetic sexual differences, since there is only one kind of individual. The differences between the male and the female *organs* of a monoecious organism can not be genetic differences, since all cells of one individual contain the same chromosomes and the same genes. It should be clearly realized that by *sex-determination* we mean the determination of *differences between individuals*, not between organs of the same individual. There are a few dioecious organisms (certain kinds of worms) in which there are no genetic differences between males and females; *i.e.*, any zygote may develop into either a male or a female, depending on certain environmental factors. These cases, however, seem to be quite exceptional. In the great majority of dioecious organisms the sexual differences are determined by hereditary factors; *i.e.*, each zygote is definitely either male or female from the moment of fertilization, depending on what sets of genes it has received from the two gametes which combined to form it, even though the sexual differences, aside from those of the chromosomes themselves, may not become *visible* until much later in development.

Heredity in asexual reproduction.—In reproduction by fission or budding, the new individuals contain exactly the same sets of chromosomes and of genes as their parents, since all the cells of the offspring are derived from those of the parents by regular mitotic divisions. All individuals thus derived from one original individual are, therefore, genetically identical, just as all the cells of a single individual are. In these asexual methods of reproduction, then, the mechanism of heredity tends to produce a group of identical individuals, while in sexual reproduction, as we have seen, genetic differences are usually to be expected even among closely related individuals.

Advantage is taken of this difference between asexual and sexual reproduction in the propagation of many kinds of plants, *e.g.*, fruit trees. A desirable variety of fruit is always propagated by asexual methods—*i.e.*, by cuttings and grafting—which result in maintaining its characteristics uniform. Propagation by seed, even with self-pollination, would usually result in much greater variation among the offspring, since the plant may be heterozygous for many genes which would be recombined in various ways by reduction and fertilization.

In dioecious organisms, all individuals derived by fission or budding from one original individual are always of the same sex, since they all contain the same set of chromosomes. This is shown, for instance, in all cases of polyembryony (p. 419), all the individuals derived from a single egg being always of the same sex. *Identical twins* in man are, as previously mentioned, produced in this way, *i.e.*, by fission of the embryo in a very early stage of development. Twins of this type are always of the same sex and resemble each other very closely in every way; this close resemblance extends to mental as well as visible characteristics. Not all human twins, however, are of this type; *fraternal twins*, produced from separate eggs which happen to be fertilized simultaneously, may be of either the same or different sexes and resemble each other no more closely, on the average, than any other brothers and sisters.

In parthenogenesis and related methods of asexual reproduction (apogamy and apospory in plants), the phenomena of heredity differ in different cases, depending on the behavior of the chromosomes in each case. In cases of diploid parthenogenesis where there are no reduction divisions or other irregularities of chromosome distribution, all the phenomena of heredity are exactly the same as in fission or budding. In cases of haploid parthenogenesis all the genes show the phenomena of sex-linked inheritance, as previously explained. In cases where one chromosome is eliminated from the male-producing eggs (as in the aphids and some other animals), the genes in this particular chromosome show inheritance of the sex-linked type, while all the others are inherited as in other asexual methods of reproduction.

In some of the simplest organisms—*e.g.*, bacteria and some protozoa—the phenomena of cell division, it will be recalled, differ more or less widely from the regular process of mitosis (p. 359). In these cases we do not know whether the individual genes are divided and regularly distributed to the daughter cells at each cell division. If they are not, we should expect corresponding irregularities in the phenomena of heredity. Heredity has, however, been very little studied as yet in these organisms.

Cytoplasmic inheritance.—All the phenomena of heredity described in the preceding pages indicate that the hereditary characteristics of organisms are determined by hereditary factors, or genes, located in the chromosomes and transmitted from cell to cell and from parents to offspring in accordance with the microscopically visible behavior of the chromosomes. There are, however, a few exceptional cases in which hereditary factors are transmitted through the cytoplasm of the cells independently of the distribution of the chromosomes; this is called *cytoplasmic inheritance*, the term cytoplasm being used, in this connection, to include everything in the cell except the chromosomes. The only proven cases of cytoplasmic inheritance are those of certain characteristics of the *plastids* of some plants. These intracellular bodies, it will be recalled, can be seen, in some cases at least, to grow and divide independently of the divisions of the cell as a whole (p. 25). At the time of cell division, the plastids are distributed approximately equally among the two daughter cells, but this distribution is a purely random one; *i.e.*, there is no mechanism for their exactly equal distribution as there is for the chromosomes. Plastids are also transmitted from parent to offspring through the egg-cell, and also, in some cases, through the pollen.

In many species of plants there are hereditary differences among the chloroplasts in regard to the amount of chlorophyl, or the time at which it is produced, in them. These differences result in corresponding differences in the color of the leaves; *i.e.*, leaves, or parts of leaves, whose plastids contain little or no chlorophyl are yellow or almost white, those with more chlorophyl are green. In most species these color differences are inherited in the usual way; *i.e.*, the production of chlorophyl in the plastids is determined by genes in the chromosomes. In some plants, however, the color of the plastids is determined, in part at least, by the origin of the plastids themselves. An example of this is the

Four-o'clock (*Mirabilis jalapa*). In one race of this species the leaves are checkered, containing patches of green and of white. The relative amounts of green and white vary on different leaves and branches of the same plant; some leaves and some whole branches are entirely green, some others entirely white. If the flowers on an entirely green branch are self-pollinated they produce only entirely green offspring, and all the descendants of these are entirely green. Flowers on entirely white branches give, when self-pollinated, only entirely white offspring; these all-white plants never survive to maturity, because of lack of chlorophyl. Flowers on the checkered branches give, when self-pollinated, some green, some checkered, and some white offspring, the proportions of these different types varying according to the relative amount of green in the branch on which the flowers grew. When flowers on one kind of branch are cross-pollinated with pollen from a different kind of branch (on the same or another plant), the results are in every case the same as though the maternal flower had been self-pollinated; *i.e.*, these color differences are inherited *from the mother only*. This result is due to the fact that the plastids are transmitted, in this species, through the egg-cell only, not through the pollen. The germ cells, as well as the somatic cells, on all-green branches contain only green chloroplasts, those on all-white branches only white ones. On checkered branches some cells contain only green plastids, some only white ones, some both kinds. These differences are due to the random distribution of the plastids among the daughter cells at cell division; *i.e.*, from a cell that contains both kinds of plastids it will occasionally happen that one daughter cell receives, by chance, only green or only white ones, in which case all the descendants of this cell will contain only the one kind. This is true of both somatic and germ cells on checkered branches, so that some egg-cells on such branches will contain only green, some only white, and others both kinds of plastids. The essential point in all this is the fact that each cell, each branch, and each plant contains only the kind, or kinds, of plastids originally transmitted to it. In other words, each kind of plastid reproduces *its own kind*, by growth and divisions. The difference between the white and the green plastids must therefore be determined, in this case, by hereditary factors located in the plastids themselves. These factors may properly be called genes, since they are, like the genes in the chromosomes, self-perpetuating bodies or substances which determine hereditary characteristics of the organism.

In some other kinds of plants, plastids may also be transmitted through the pollen grains, entering the egg-cell from the pollen tube along with the sperm nucleus. A case of this kind is the plant Pelargonium. Here the facts as to inheritance of leaf color are similar to those in Mirabilis, except that cross-pollination of flowers on green branches by pollen from white branches, or vice versa, gives checkered offspring, showing that these zygotes receive both kinds of plastids. In this plant, therefore, leaf color is inherited from both parents. The two cases, however, are essentially similar in that the color of the plastids is determined by hereditary factors, or genes, in the plastids themselves.

These cases of plastid inheritance, although exceptional, show that any component of the cell which is self-perpetuating—*i.e.*, grows and reproduces itself specifically—and is transmitted from cell to cell, may act as a hereditary factor, or gene. This raises the question whether there may be other cytoplasmic hereditary factors aside from plastids. Such factors, if there be any, must show the same general characteristics as plastid inheritance, in contrast to the regular phenomena of chromosomal—or, as it is commonly called, Mendelian—inheritance. That is, such cytoplasmic factors would not conform to the regular laws of heredity—which, as we have seen, are due to the behavior of the chromosomes at mitosis and maturation—and they would not, of course, be linked to any group of chromosomal genes. Except in the cases of plastid inheritance such as those described above, no such factors have been found in any organism in which heredity has been studied. In those organisms in which heredity has been studied most thoroughly—especially Drosophila melanogaster—every hereditary factor studied is found to occupy a definite locus in one of the linkage groups, *i.e.*, to be located at a definite position in a particular chromosome. In other organisms, in which linkage relations have been less studied, every hereditary factor studied (with the exceptions noted above) is found to be transmitted according to the Law of Segregation, which proves it to be located in some chromosome. While there *may* be other cases of cytoplasmic inheritance, they must be relatively rare. All the evidence at present available indicates that, except for a few cases of plastid inheritance in plants, *all* the hereditary characteristics of organisms are determined by genes located in their chromosomes.

Nature of the genes.—Genes, like enzymes and vitamins, are known by what they *do;* we know very little about what they *are.* The definitely established facts, derived from the study of heredity, may be summarized briefly: the genes are stable, self-reproducing bodies, located at definite constant positions in the chromosomes, by which they are transmitted in a very regular manner from cell to cell and from parent to offspring through the germ cells, and these bodies determine, through the processes of development, all the hereditary characteristics of the organism.

Our knowledge of the composition and structure of the genes is very indirect and, as yet, very vague. The only clue we have as to their chemical composition is derived from chemical analysis of the chromatin, which we know contains the genes. The head—*i.e.*, the nucleus—of the sperm-cell is composed almost entirely of chromatin (p. 387), and we know that each sperm-nucleus contains a complete haploid set of genes. Sperm-cells can be obtained in large quantities from some animals, and the heads can be separated from the tails. Chemical analysis of the sperm heads from a number of different animals shows them to be composed entirely, or almost entirely, of *nucleoproteins.* These substances are conjugated proteins, composed of nucleic acid and simple proteins (p. 54). The nucleic acid is probably the substance which combines with "nuclear stains," giving the chromatin its distinctive staining properties by which we recognize it microscopically. This substance also has a very marked power of *gelation*, even in rather weak solutions, a property which probably contributes to the structural stability and relatively solid consistency of the chromosomes. There are two slightly different nucleic acids, having the formulas $C_{38}H_{49}O_{29}N_{15}P_4$ and $C_{43}H_{51}O_{29}N_{15}P_4$ respectively,[1] found in different organisms; but so far as known there are not more than two—certainly, at most, a very few—different nucleic acids. It therefore seems very improbable that the genes are composed entirely of nucleic acid. It is quite possible that the nucleic acid merely forms a framework or "skeleton" of the chromosomes, to which the genes are attached, presumably by chemical combination with it. The simple proteins combined with the nucleic acid in the sperm head may be of many different kinds. As we have seen (p. 54), a practically infinite number of chemically distinct proteins can be formed by different proportions and different arrangements of the various amino-acids in the protein molecules. Present methods of chemical analysis enable us only to analyze the chromatin in bulk and to determine approximately the proportions of the various amino-acids present. Such analyses show characteristic differences in the protein components of the chromatin of different species of animals, although the nucleic acid is apparently identical in all of them. As to differences between different chromosomes or different parts of a chromosome, in any one kind of sperm, chemical analysis is at present unable to supply any evidence. We can only say, therefore, that the characteristic properties of different genes may be due to chemical differences in the proteins of which they are composed, but this is not yet proved. If the genes be composed, wholly or in part, of any substances other than simple proteins and nucleic acid, these other substances must be present in proportions so small as to have hitherto escaped detection by chemical analysis. Summarizing our present very meager evidence on the chemical nature of the genes: they are probably composed of nucleoproteins, and the qualitative differences among the genes, manifested in the different hereditary characteristics they produce, may perhaps be ascribed to different proportions and arrangements of the various amino-acid radicals (and possibly other radicals) in these proteins.

---

[1] The formula of this second nucleic acid is not yet entirely certain. The nucleic acids are made up of phosphate, monosaccharose, and nitrogenous (basic) radicals; they are synthesized from these simpler compounds in the cell, and are decomposed into them by hydrolysis.

Another question which can be attacked only very indirectly is the *size* of the genes. The *number* of genes, in Drosophila melanogaster, can be estimated, rather roughly, by two different methods. One method is to divide the total map-length of the whole set of chromosomes by the estimated map-distance—*i.e.*, the cross-over value—between adjacent genes. Cross-over values as low as 0.1% are found in a number of cases, in various regions of the chromosomes. Values smaller than this are found in only one region (the 0 end of the *X*-chromosome), and there is reason to suppose that there is something unusual about the cross-over relations in this region. Accepting 0.1 unit, then, as a probable average map-distance between adjacent genes, and dividing this into the total map-length of the four chromosomes, about 300 units, we obtain about 3,000 as the total number of genes in each haploid set of chromosomes. This is, of course, only a very rough estimate, since we do not really know how much the map-distance between adjacent genes may differ in different regions of the chromosomes. Another, entirely different, method of estimation (based on the frequency of recurrence of *mutations* [p. 567] of the genes) gives about 2,000 as the *minimum* number of genes in a haploid set. In view of the approximate agreement of these two methods, we may accept, tentatively, the rough estimate of between 2,000 and 3,000 as a probable value of the number of genes in each haploid set of chromosomes in this organism. Since we know that each sperm-nucleus contains a complete haploid set of genes, this number of genes must be contained within the volume of the sperm head. This volume, which can be approximately determined by microscopic measurements of the sperm head, agrees fairly well with the total volume of a haploid set of chromosomes calculated from measurements of their lengths and thickness: about 0.25 cubic micron. If the chromosomes are composed entirely of the genes, then the average size of a gene must be equal to *volume of chromatin* ÷ *number of genes*. This method of computation gives $\frac{0.25}{2500} = 0.0001$ cubic micron (approximately) as the average volume of a single gene; its diameter (assuming the gene to be spherical or approximately so) would thus be about

$0.06\mu = 6 \times 10^{-6}$ cm. Since, however, we have no idea as to what proportion of the chromatin is actually composed of the genes, these figures merely represent the *maximum possible* size of the genes: they may be very much smaller—how much, we have as yet no method of estimating. These calculations, rough as they are, demonstrate quite conclusively that the individual genes are ultramicroscopic in size, *i.e.*, below the utmost limit of true microscopic visibility (p. 60). On the other hand, the figure arrived at for the maximum diameter of the gene is about ten times as great as the probable diameter of the largest known protein molecules (about 6×10^{-7} cm.); *i.e.*, the maximum volume of the gene is about 1,000 times that of the largest protein molecules. This may mean that each gene contains 1,000 or more molecules; but, on the other hand, it may mean that only $\frac{1}{1000}$ or less of the total volume of the chromatin is actually composed of the genes. The evidence at present available on the size of the genes, therefore, affords no indication of whether each gene is a single molecule or is composed of several or many molecules.

All the facts of heredity emphasize the *stability* of the genes; *i.e.*, the persistence of each gene through generation after generation, unmodified by other genes present in the same cell or by any other surrounding conditions. Indeed, the whole existence of hereditary resemblance among related organisms depends on the stability of the hereditary factors. This stability of the individual genes is, however, not absolute: genes occasionally, though very rarely, change; this phenomenon is called *mutation* (p. 567). We know, as yet, very little about the nature or causes of these changes. In general, however, mutation seems to be a sudden, definite, and complete change, affecting only a single gene but apparently affecting the whole of that gene simultaneously; the new gene thus produced being (at least usually) just as stable, from the moment the mutation has occurred, as the original gene from which it arose. Even when the mutation occurs in a homozygous diploid cell, only one of the two identical allelomorphic genes mutates. These facts seem to suggest that the gene is a single molecule or something comparable to it; *i.e.*, a definite, unified structure which reproduces, is transmitted, and changes, when it does change, *as a whole.*

The most essential property of all genes is that of specific self-multiplication. When we cross two races, *e.g.*, the white and black Andalusian fowls (p. 460), the *F1* zygote contains *one* of each of the genes *B* and *b*. This zygote produces millions of cells, each diploid cell containing one of each of these genes, and each gamete containing one or the other of them. The same is true of every other gene in the zygote, for all the genes found in each cell of the organism are identical (except for the very rare occurrence of mutation) with those originally present in the unicellular zygote. When a gene mutates—changes into a different gene—every cell descended from that in which the mutation occurred contains one gene of the new kind. These facts obviously mean that each gene determines the production of more genes exactly like itself. This kind of phenomenon is found in certain chemical reactions in non-living systems, where a particular substance catalyzes a reaction resulting in the production of more of that substance; this phenomenon is called *autocatalysis.*

The property of self-multiplication—*i.e.*, growth and reproduction—is one of the most fundamental characteristics of living organisms. No cell or part of a cell can grow or reproduce unless it contains a nucleus or nuclear material, *i.e.*, chromatin (p. 23). All organisms, even the very smallest microscopically visible bacteria, contain chromatin, *i.e.*, nucleo-protein, as shown both by staining tests and by chemical analysis. The facts of heredity prove conclusively that the chromatin is composed, in part at least, of genes, each of which has the power of specific self-multiplication. Except for the special cases of plastids described above (p. 509), there is no proof that any other component of the cell or the organism has this power. So far as our present knowledge goes, therefore, it strongly suggests that the genes—located, with very few exceptions, in the chromosomes—alone have the power of specific self-multiplication, and that all other components of the cell are products of the activities of the genes, just as all extra-cellular components of the organism are products of the activities of the cells.

The genes can grow and reproduce only in the proper environment; *i.e.*, in the protoplasm of the same species, or a fairly closely related species, of organism. In some cases an egg-cell of one kind of organism can be activated by a sperm of a very different kind (*e.g.*, of a different class or phylum), but in such cases there is no true fertilization, and the chromatin of the sperm plays no part in the development of the egg; *i.e.*, the genes introduced by the sperm apparently cannot live and multiply in the foreign cytoplasm. The relation of the cytoplasm to the genes thus seems to be similar to the relation of the blood to the cells in higher animals, *i.e.*, a medium produced by them and providing the necessary environment for their continued life and growth.

It may be not without significance that the estimated maximum size of the gene corresponds rather closely with that deduced, by entirely different methods, for the filterable viruses (p. 28)—ultramicroscopic organisms whose existence is detected by exactly the same properties as those of the genes: their ability to multiply and to produce detectable effects in their environment. It seems, therefore, not illogical to regard these ultramicroscopic organisms as *free genes*, *i.e.*, genes without cytoplasm or other incidental cell structures. Such organisms represent probably the simplest, and perhaps the earliest, form of life.

Phenotypic effects of the genes.—The existence and properties of the genes are inferred from the visible, or otherwise detectable, effects they produce in the organism containing them, *i.e.*, their *phenotypic* manifestations (p. 470). Between the genes in the unicellular zygote and the phenotypic characters of the adult organism lies the whole complex series of processes called, collectively, *development*. The question of the mechanism of development—which is, in large degree, the question of *how* the genes produce their phenotypic effects—will be treated in the following chapter. For the study of *heredity* as such, the visible hereditary characteristics of the organism are simply convenient indicators of the presence of certain particular genes, or particular combinations of genes, in its cells.

In the preceding sections we have selected as examples characters which are sharply marked and easily detectable, such as color, form, or size of externally visible structures. Such characters were chosen as a matter of convenience and simplicity. Further study, however, shows that many other kinds of characters are affected by particular genes: internal as well as external structures, the behavior of organisms—reflexes, instincts, and intelligence,—general functional characteristics such as rate of development, viability, fertility, etc. These effects may be of any extent, from very slight effects, detectable only by careful measurements, to very great effects, profoundly influencing the appearance, structure, behavior, or viability of the organism. In short, every characteristic, structural or functional, of an organism is affected in various degrees by various genes in the organism.

Each gene, moreover, may affect several or many characteristics of the organism. For instance, we have used as an example in one of the preceding sections (p. 502) a gene producing white eyes in Drosophila. We picked this particular effect of the gene, to follow its inheritance, because it is very easily seen and sharply marked. Further study, however, reveals many other effects of this same gene: the flies homozygous for it also lack color in some of the internal organs which would otherwise be pigmented, they develop somewhat more slowly than the red-eyed flies, produce fewer offspring, and are less able to survive under unfavorable conditions. What is true of this gene is also true of many, probably all, other genes: each gene affects, in various ways, many different parts and functions of the organism. When we speak of a "gene for white eyes," a "gene for short wings," etc., we are merely using, to identify the gene, one of its most obvious and conspicuous effects.

Conversely, each part and characteristic of the organism is affected by many genes. There are, for instance, at least fifty different genes known to affect the eye-color of Drosophila. The eye-color of any particular individual is determined by the genes present in all these different loci and perhaps in others of which we still know nothing. When we speak of a cross between red-eyed and white-eyed flies as a "one-factor cross," it is assumed that both races are homozygous and similar for all other genes affecting eye-color; *i.e.*, we are studying, deliberately, the inheritance of one single genetic difference. If we cross two flies differing in many genes affecting eye-color, we shall obtain, in the *F2* and subsequent generations, a great many different eye-colors, produced by the various possible recombinations of these various genes. The same is true of other characters, such as body-color, size and shape of wings, size, vigor, viability and fertility of the flies, etc. Each characteristic, structural or functional, of the organism is affected by many distinct genes.

Summarizing, we may say that the whole organism is the product of the action and interaction of all its genes; each gene may affect many, or perhaps all, parts and functions of the organism, and each part or process may be affected by many, or perhaps all, of the genes. Nevertheless, certain parts are affected more, or at least more obviously, by some genes than by others; and certain genes produce their most striking effects on particular characteristics of the organism; these particularly striking effects are chosen, as a matter of convenience, to identify the gene in studying its hereditary transmission.

Heredity in man.—The direct study of heredity in man presents considerable practical difficulties. The greatest of these is the impossibility of experimental breeding, by which all our accurate knowledge of heredity in other organisms has been obtained. Our only source of data on human inheritance is the observation of the appearance of particular characteristics in family pedigrees, which is in many respects a very unsatisfactory method of study. Other difficulties are the very slow rate of breeding and the small number of offspring of each mating. The large number of chromosomes—24 pairs—also renders it difficult to study linkage. Another serious difficulty is the impossibility of accurately controlling environmental factors, so that it is often impossible to tell what part of the observed results is due to environmental rather than genetic factors.

Despite all these difficulties, enough has been learned of human heredity to show that the general laws and mechanisms are the same as in other organisms. Heredity has also been studied in various other mammals—mice, rats, rabbits, guinea-pigs, etc.—which are somewhat more favorable for this purpose, and found to be exactly the same, in general principles, as in Drosophila, plants, etc.

Most of the normal differences among human individuals —*e.g.*, height, weight, color of skin, hair, eyes, etc.—are, as in other organisms, affected by many genes. Since there are no pure races in man—*i.e.*, all individuals are heterozygous for many genes—it is difficult to analyze the genetic factors involved in the determination of such characters. Many of these characters, especially height and weight, are also greatly affected by environmental factors, such as nutrition. In the case of eye-color, which is relatively little affected by environmental factors, it has been possible to analyze the genes involved fairly satisfactorily. Blue eye-color is inherited as a simple recessive. The various shades of dark eye-color (*i.e.*, any color other than blue) are determined by several other pairs of genes, the darker allelomorph of each pair being usually dominant to the lighter. The various eye-colors called green, gray, hazel, brown, and "black" (very dark brown) are determined by different combinations of these genes, produced by segregation and independent assortment (or perhaps, in some cases, by crossing-over, their linkage relations being yet unknown). The colors of skin and hair seem to be more complex genetically, and have not yet been satisfactorily analyzed, though there is no doubt that they are determined chiefly by genetic factors. Such characters as height and weight are still more difficult to analyze genetically, because of the great influence of environmental factors; we can only say that there are some genetic factors involved, because of the positive correlation (*i.e.*, more or less marked similarity) between parents and offspring, and between offspring of the same parents, in regard to these characters. Some other characters, such as certain kinds of differences in the blood, have been proved to be purely genetic, and their inheritance analyzed in terms of a small number of genes.

The most striking one-factor cases in human heredity are those of various abnormal conditions. By an "abnormal" character we mean simply one which is relatively rare and usually more or less deleterious to the individual possessing it. Such abnormalities, which have been shown to be determined wholly or chiefly by a single pair of allelomorphic genes in each case, are polydactyly (extra fingers and toes), brachydactyly (abnormally short fingers and toes, due to missing segments), albinism (absence of pigment from skin, hair, and eyes), certain kinds of dwarfism, and a number of others. A number of abnormalities are sex-linked: among these are color-blindness and hemophilia ("bleeding," due to failure of the blood to coagulate in cuts). Both these characters are recessive, and are inherited exactly as are sex-linked recessives (*e.g.*, white eyes) in Drosophila. This proves the mechanism of sex-determination to be the same in man as in Drosophila and in most other animals, which is confirmed by microscopic evidence, the male having a visibly unequal *XY* pair,[1] the female two *X*-chromosomes.

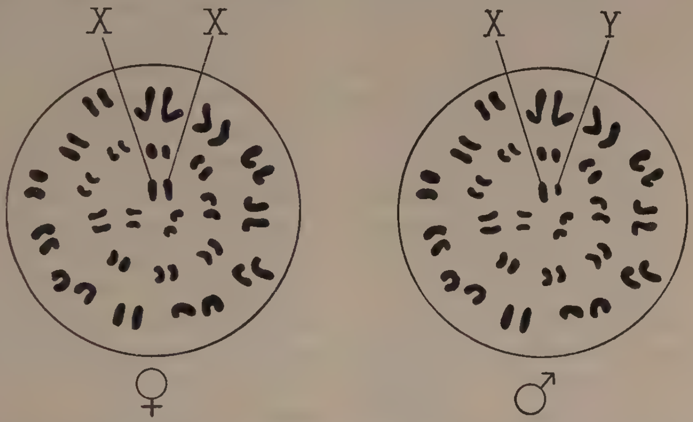


FIG. 172.—Diploid chromosome groups of man. The arrangement of the chromosomes in these figures is diagrammatic. (Adapted from Painter.)

Aside from sex-linked genes, no other cases of linkage are definitely known in man; this is due to the large number of chromosomes and the impossibility of experimental breeding. In some other mammals, however, linkage has been studied and found to be essentially the same as in Drosophila, except that crossing-over occurs equally in both sexes, as is also the case in some (perhaps most) other animals and in plants. In short, the laws and mechanisms of heredity, discovered chiefly by experiments on Drosophila, apply, with but minor differences in some details, to man as well as to all other sexually reproducing organisms.

---

[1] Some observers have described the human male as having no *Y*-chromosome, but a single unpaired *X*; this may be due to overlooking the very small *Y*-chromosome, or it may be that in man, as in some other animals, the *Y*-chromosome may be absent in some individual males.

Of more practical importance, perhaps, than most of the visible characters mentioned above is the question of the inheritance of mental characteristics. This problem presents even greater difficulties: the difficulty of accurately measuring mental characteristics and the difficulty of distinguishing between the effects of genetic and of environmental factors on them. The first of these difficulties has been overcome, to some extent at least, in recent years, by the use of "intelligence tests," which seem to give a fairly reliable measure of individual differences in respect to certain types of response, somewhat arbitrarily called "intelligence." [1] It is, however, extremely difficult to determine how much of these differences in intelligence, as thus measured, is due to genetic, and how much to environmental, factors. The best evidence on this question is derived from the study of *identical twins*. Twins of this kind, it will be recalled, are derived from a single zygote and are therefore necessarily *identical in all their genetic factors* (p. 419). Such twins are always of the same sex, and resemble each other very closely in every way, often being almost indistinguishable. The best evidence on the respective effects of genetic and environmental factors is derived from the study of identical twins who have been raised under different environmental conditions. A number of such cases have been studied, and it is found that the twins always show a very high correlation (*i.e.*, a strong resemblance) in intelligence as measured by the intelligence tests. This strongly indicates that intelligence, in this sense, is largely determined by genetic factors. In some other mental characteristics, such as are commonly designated by the terms "character" and "personality," these twins show less correlation; this may mean that the methods of testing these qualities are less reliable, or it may mean—as we should, perhaps, judge from our general experience—that these characteristics are more susceptible to modification by environmental factors.

The results of intelligence tests also show a marked correlation—though less than in identical twins—between parents and offspring, and between offspring of the same parents. It must not be overlooked, however, that, in general, environmental conditions as well as genetic factors are more similar for such closely related individuals than for the population as a whole. Subnormal mental conditions, such as some forms of insanity, feeble-mindedness, etc., often show a marked tendency to "run in families," and the same is true of supernormal mental abilities. In all these cases, again, it is difficult or impossible to distinguish between the effects of genetic and of environmental factors. We are only justified in saying, on the basis of our present knowledge, that mental as well as visible characteristics are undoubtedly largely determined by genetic factors; but as to details—what and how many genes are involved in any particular case, and to what extent their effects may be modified by environmental factors, such as nutrition, disease, education, social and economic conditions, etc.—we still know very little.

---

[1] This use of the word "intelligence" is a more restricted, and also a less accurately definable, one than the general definition given in Chapter XVII.

The laws of heredity, recent as their discovery still is, have already proved of enormous practical value in the improvement of domestic animals and plants by selective breeding. It is natural to suppose that the human species, in which the general laws of heredity are the same, might be improved by the same methods. Our knowledge of human inheritance is, however, as has been emphasized above, still very meager in detail—to say nothing of the difficulty of deciding what qualities are desirable to "breed for" in man. The inherent difficulties of the subject have, unfortunately, been still further enhanced by the fact that many of the supposed "authorities" on human inheritance are extremely uncritical and unscientific and often appear to have "some axe to grind." In contrast, the foremost scientific students of genetics, realizing the enormous difficulties in the study of human heredity and the meagerness of our present detailed knowledge, are of the opinion that the greatest hope of human advance, at least in the near future, still lies in the amelioration of environmental conditions rather than in "selective breeding" of human beings.

CHAPTER XXIII

THE MECHANISM OF DEVELOPMENT

ONE of the most striking differences between an organism and any kind of artificial machine is that the living machine *builds itself*, so to speak. This phenomenon is particularly striking in the higher, multicellular organisms, where each individual passes through a continuous series of changes from a minute, relatively simple, single cell to a much larger, more complex, multicellular structure. This whole series of changes, involving processes of growth, cell division, chemical and structural differentiation, is called *development*. In previous chapters (XX, XXI) we have described briefly the visible structural changes in the development of various multicellular animals and plants. In the present chapter we are concerned with the *mechanism* of development, *i.e.*, its causative factors and how they operate.

The factors involved in the development of any organism may be divided into two groups: *genetic* and *environmental* factors. By genetic factors we mean self-perpetuating bodies or substances which are transmitted from generation to generation through the germ-cells; *i.e.*, the genes. Under the term environmental factors we include everything else which may affect the organism in any way at any stage of its development. We are all familiar, from our general experience, with the fact that the course of development in any particular organism is determined chiefly by its hereditary endowment: the fertilized egg of a chicken develops into a chicken, that of a dog into a dog, that of an oak into an oak, etc. Not only the distinctive characteristics of different species of organisms, but also those of different varieties or races, and even many of the differences between closely related individuals, are determined by their genes, as we have seen in the preceding chapter. Hence, one of the central problems of development is that of how the genes influence the processes of development so as to produce the distinctive characteristics of the organism. In the study of *heredity*, which is concerned solely with the *transmission* of genetic factors from generation to generation, the phenotypic characteristics of the organism are used simply as "indicators" of the presence of particular genes or combinations of genes; in the study of *development*, on the other hand, the essential questions are: *when*, *where*, and *how* do the genes produce their effects?

The importance of environmental factors in development is more easily overlooked, simply because we usually take them for granted. A moment's consideration, however, will make it obvious that such factors as oxygen, water, and food supply, temperature, the osmotic pressure and chemical composition of the surrounding medium, etc., play absolutely essential rôles in the development of any organism. Any considerable variation in any of these factors may modify the course of development or prevent it entirely. The characteristic effects of any particular combination of genes can be produced only under a particular set of environmental conditions; hence every phenotypic character of an organism must logically be regarded as a product of the interaction of certain genetic and certain environmental factors. In many cases, the effects of differences in environmental factors are indistinguishable, in appearance, from the effects of genetic differences (p. 540).

Between the genes in the nuclei and the environment affecting the organism from outside, it would seem that we have left out of account a very essential factor in the processes of development, *viz.*, the *cytoplasm* of the cells. In fact, the visible processes of development, as well as their underlying chemical changes, take place largely in the cytoplasm; the composition and structure of the cytoplasm at any moment must therefore be among the most important factors in determining what happens next. The cytoplasm, however, at each stage of development, is the product of the activities of the genes and of environmental factors during previous stages. We can carry this right back to the zygote at the moment of fertilization; its cytoplasm is derived from that of the gametes (chiefly, or perhaps in many cases entirely, that of the egg-cell), which in turn has been produced by the action of the genes and of environmental factors in the parent organisms. The cytoplasm must therefore logically be regarded in the same category as the blood, internal secretions, cell walls, etc.—as a product of the developmental processes rather than a primary determining agent of them. The cytoplasm together with the intercellular materials—*i.e.*, everything inside the organism except its genes—may be called, collectively, the *internal environment*, in contrast to the *external environment* outside the organism.

When do the genes produce their effects?—Evidence from both genetic and embryological experiments shows that the primary effects of particular genes on developmental processes may be produced, in different cases, at various stages of the life cycle: before maturation of the gametes (specifically, of the egg-cell), after maturation but before fertilization, or after fertilization, either early or late in the development of the zygote.

If certain genes produce their effects before maturation of the egg-cell, the corresponding characteristics of the zygote will be determined by the genetic constitution of the mother—*i.e.*, by the genes present in the diploid germ cells of the mother before the reduction division—rather than by its own genetic constitution, *i.e.*, the genes present in the zygote itself. A number of cases of this kind are known, usually involving only characteristics of the early embryo. For instance, in the silkworm moth, there are two races differing in the color of the embryo, which can be seen through the transparent egg-shell. When these two races are crossed, the color of the *F1* embryos is always like that of the race to which the *mother* belongs, regardless of which way the cross is made. But when these *F1* individuals are raised and bred, the color of the *F2* embryos is determined by the dominant gene of their heterozygous mother, regardless of whether this gene came from her mother or her father in the original cross. If the *F2* females, in turn, are bred, three-fourths of them give embryos with the dominant color, one-fourth give embryos with the recessive color, all the embryos derived from any one mother being alike (Fig. 173). These results may be summarized thus: the color of the embryo is always determined by the genetic constitution of its mother, all embryos from *CC* or *Cc* mothers (*i.e.*, mothers homozygous or heterozygous for the dominant gene of the pair involved) showing the dominant color, those from *cc* mothers showing the recessive color, regardless of the embryo's own genetic constitution. This shows that the color of the embryo is determined by some effect produced by these genes upon the cytoplasm of the germ cells (oogonia or oocytes) before reduction and fertilization. Either the pigment is present in the oocyte before maturation, scattered in the cytoplasm, and later, during early embryonic development, collects at the surface of the embryo; or else there must be present in the cytoplasm of the oocyte some uncolored substance which later produces a particular kind of pigment in the surface of the embryo. In either case, the gene brought in by the sperm has no effect on the development of this pigment in the *F1* embryo, but it does produce its effect (if dominant) on the oocytes of these heterozygous *F1* individuals when they have become adults. This kind of result is called "maternal

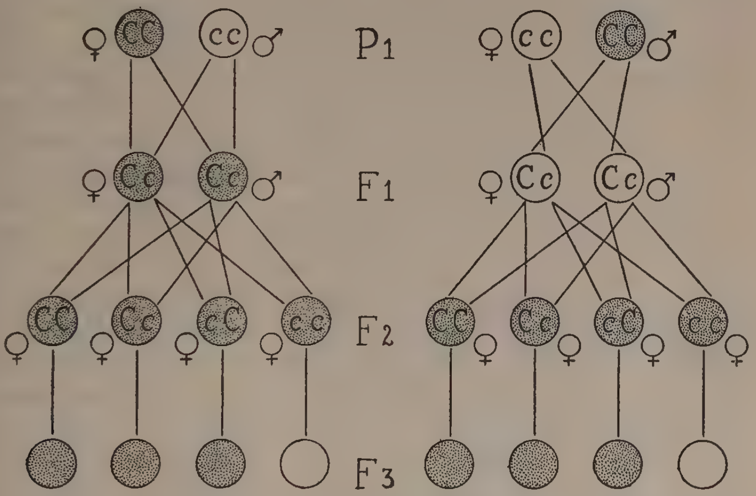


Fig. 173.—Diagram illustrating "maternal inheritance" of embryonic color in the silkworm. Shaded circles represent embryos showing the dominant color, white circles those showing the recessive color; the letters indicate the genetic constitutions of these individuals. (The fathers and the genetic constitutions of the *F3* are not indicated in the diagram, as they do not affect the color of the *F3* embryos.)

inheritance," though this term is really a misnomer, since the *inheritance* of the genes determining the color of the embryo is from both parents equally; the only difference between this case and any other one-factor cross (p. 460) is in the *time* when the genes produce their effects on the cytoplasm.

These maternal effects are usually found only in the early stages of development, but in a few cases they may persist even to the adult stage. One case of this kind is found in certain snails. In some species of snails the direction of coiling of the shell is always right-handed, in some species it is always left-handed, but in some other species both right-handed and left-handed individuals occur. When the two kinds of individuals are crossed, the direction of coiling is found to be inherited as a one-factor difference, right-handedness being dominant to left-handedness, but the direction of coiling in each individual is determined by the genetic constitution of its *mother* rather than by its own genetic constitution; *i.e.*, all the offspring of *RR* or *Rr* mothers are right-handed, all those of *rr* mothers are left-handed, regardless of which genes these offspring themselves contain. Just as in the case of the silkworm moths described above, the gene brought in by the sperm seems to exert no effect on the phenotypic character of the *F1* individual, but does produce its effect (if dominant) on the egg-cells produced by the *F1* individual. Here again, the effect of the genes on the cytoplasm must be produced before maturation of the egg-cells, since the character of the offspring is determined by the genes present in the *diploid* cells of the mother. That this case is really very similar to that of the silkworm embryo is shown by studying the development of the snails. The direction of coiling is, in fact, not merely a characteristic of the shell, but extends to all the internal organs of the animal. This asymmetrical structure can be traced back, through the developmental stages, to the early cleavage divisions of the zygote. The cleavage divisions are asymmetrical, of a spiral pattern, and the difference between right-handed and left-handed individuals appears at least as early as the second cleavage division, and perhaps even in the first. These facts indicate that there is some asymmetrical structure in the cytoplasm of the zygote, which has been derived from the cytoplasm of the oocyte unchanged by reduction and fertilization. In other words, the gene brought in by the sperm has not had *time* to affect the cytoplasmic structure before the early cleavage divisions by which the asymmetry of the individual is irrevocably fixed.

Similar maternal effects are often found in crosses between different species of animals which differ markedly in the early developmental stages. Such interspecific crosses have been studied chiefly in sea-urchins and in fishes. In these cases it is quite generally found that the characteristics of the early developmental stages—the rate and pattern of cleavage, the form of the blastula and often that of the gastrula—of the heterozygote are identical with those of the maternal species. In most of these cases, however (when the visible behavior of the chromosomes is normal), the effects of the paternal genes become apparent in the later embryonic or early larval stages. These animals (the pure species as well as the hybrids) are difficult to raise and breed in the laboratory, so that *F2* progeny from these crosses have not been secured. There is no reason, however, to doubt that when they are secured the results will be the same as in the case of the snails, described above; *i.e.*, that the genes derived from the *P1* father will show their effects on the cleavage of the *F2* zygotes.

The most significant general conclusion to be drawn from these cases of maternal effects is that the genes take a considerable *time*—a matter of hours, at least, or perhaps even days in some cases—to produce their effects on the cytoplasm. This fact has an important bearing on the question of how the genes produce their effects (p. 535).

In animals the period between reduction and fertilization is so short that the genes present in the gametes can have little opportunity to produce observable effects: no such effects have yet been found with certainty. In plants, however, where the haploid stage is of longer duration, there are many clear cases of effects of the genes during this period. Even in seed-plants, where the haploid (gametophyte) stage is relatively short, as compared with the lower plants, there are many cases in which characteristics of the gametophyte are determined by the genes present in it after the reduction division. In one case, in corn, the kind of starch formed in the pollen grain is determined by a particular gene, the gene *w* ("waxy") determining the formation of a peculiar kind of starch staining red instead of blue with iodine, while its allelomorph *W* determines the production of the ordinary kind of starch. *W* is completely dominant to *w* in diploid cells, but in the pollen from heterozygous (*Ww*) plants, half the pollen grains (those containing *w*) have the red-staining starch, while the other half (containing *W*) have the blue-staining kind. This shows that the gene *w* must produce its effect after the reduction division. In many cases the viability of the pollen grain and the rate of growth of the pollen-tube are determined by the genes present in it after reduction. In some cases, also, the viability of the macrospore is determined by its own genes, *i.e.*, those of the haploid set present in it after the reduction division. In all these cases, the genes must produce their effects in the relatively short period between the reduction division and the development of the gametophyte (pollen-tube or embryo-sac).

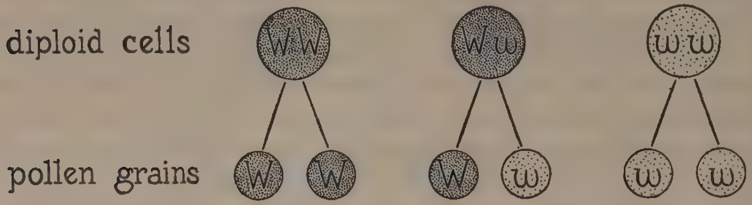


FIG. 174.—Diagram illustrating the effect of the "waxy" gene (*w*) in pollen grains. The darker shading indicates cells with blue-staining starch, the lighter shading those with red-staining starch; the letters indicate the genetic constitutions of these cells.

In most cases the hereditary characteristics of a diploid organism, whether plant or animal, are determined by the genes present in the zygote after fertilization. The exceptions to this usually involve only the very early embryonic stages, as explained above ("maternal inheritance"). Many embryonic characters, however, show the effects of the paternal genes brought in by the sperm as well as the maternal genes present in the egg-cell after reduction. We have already seen examples of such embryonic characters, determined equally by both gametes, in the pea (pp. 466, 470). In the species crosses of sea-urchins and of fishes, mentioned above, the effects of paternal genes usually become evident at the gastrula stage or a little later, which is in some cases less than 24 hours after fertilization. In Drosophila, also, there are many cases in which the development of the embryo is determined by the genetic constitution of the zygote, *i.e.*, by paternal as well as maternal genes. The total duration of this embryonic stage is about 20 hours; how early in this period the paternal genes may produce their effects has not yet been determined.

Many of the hereditary characteristics of the adult organism do not appear until relatively late in development; *e.g.*, in Drosophila most of the adult characters do not appear until the latter part of the pupal stage (p. 408). Do the genes determining these characteristics produce their effects only at or about the time when the visible characters appear, or have they produced their primary effects much earlier in development, the visible character being the end result of a long series of cytoplasmic processes? This question is closely bound up with the question of *where* the genes produce their effects, as explained below, and will be considered along with it (see Fig. 177).

Where do the genes produce their effects?—In many cases the most conspicuous visible effect of a particular gene is seen in one particular part of the body; *e.g.*, the color of the eyes, shape of the wings, etc. (p. 518). Are these effects produced by the genes present in the cells composing these parts of the body, or are they more indirect results of the action of genes in other cells? Normally, all the cells of an individual organism (except, of course, its mature gametes) contain exactly the same genes, all the genes being distributed to every cell of the body by the normal operation of the mechanism of mitosis (p. 356). Occasionally, however, this mechanism "slips a cog," resulting in irregular distribution of one or more chromosomes (p. 559). In some cases, for instance, a chromosome is lost from one cell by lagging on the spindle at mitosis and failing to be included in the daughter nucleus (Fig. 175). All the descendants of this cell will then lack this particular chromosome. Such abnormalities furnish the best evidence on the questions of when and where the genes produce their primary effects.

In Drosophila, where such cases have been most thoroughly studied, this evidence shows that in most cases the action of the genes is strictly local; *i.e.*, the hereditary characteristics of each part are determined by the genes present in its own cells. Suppose, for instance, that in an individual heterozygous for a pair of genes affecting eye-color, the chromosome carrying the dominant allelomorph happens to be lost, during development, by a cell from which the tissues of one eye are subsequently derived, so that the cells of this eye contain only the recessive allelomorph. In most cases of this kind, it is found that this eye has the color determined by the recessive gene, while the other eye, whose cells contain both allelomorphs, has the color determined by the dominant allelomorph, as usual (p. 469). This is true not only for eye-color but also for many other visible characters. Such individuals, containing patches of tissue differing genetically from the rest of the body, are called *mosaics* (Fig. 176). The patches in such mosaics are sometimes as small as a few cells or perhaps even a single cell. In such cases there can be no doubt that the gene produces its effect directly in the cells where the visible character appears or in the immediate precursors of these cells.

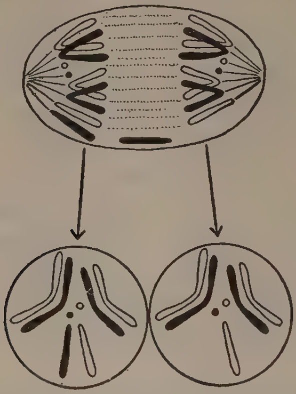


FIG. 175.—Diagram showing loss of one X-chromosome at a mitotic division in Drosophila, and the chromosomes of the two daughter cells. One member of each pair of homologous chromosomes black, the other white.

There are, however, some genes which do not work in this way. That is, in mosaics produced by chromosome elimination, the effects of these particular genes are seen even in parts of the body where they are not present. This may mean either that these genes have produced their primary effects upon the cytoplasm before they were eliminated, in the precursors of the cells where the visible results appear; or that they produce their primary effects in some other parts of the body, which secondarily affect those parts where the visible results appear (Fig. 177). In either case, the primary effects of these genes must be rather remote, in time or place or both, from the visible end results. Such

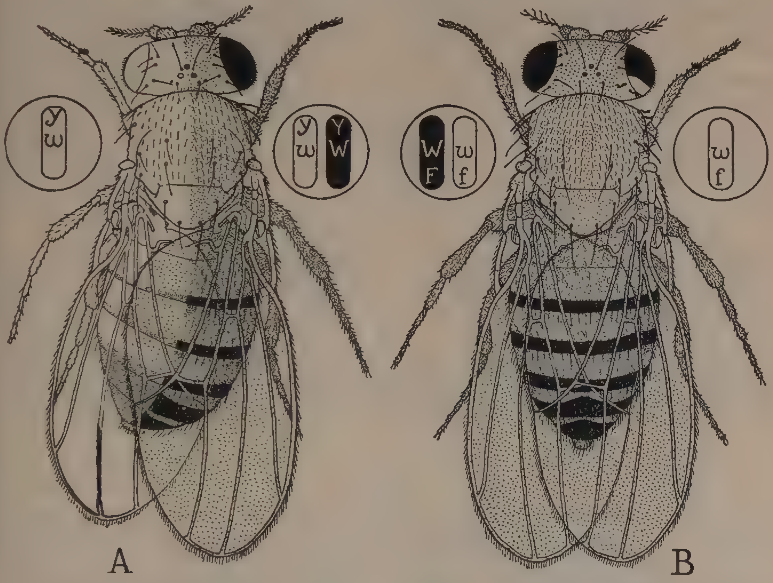


FIG. 176.—Mosaics of Drosophila. *A*, mosaic in which the whole left side is male (as shown by its smaller size, pattern of abdomen, and sex-comb on front leg) with yellow body-color and white eye, while the right side is female with "gray" body-color and red eye. The X-chromosomes of each side are shown in the circles. This mosaic is due to the loss of one X-chromosome, containing the dominant genes *Y* and *W*, at an early (perhaps the first) cleavage division, so that approximately one-half of the fly is formed of cells with only one X-chromosome, containing the recessive genes *y* and *w*. *B*, mosaic in which a small part, comprising the right shoulder, front leg, and corner of the head, is male (as shown by sex-comb) with "forked" bristles and white eye-color, while the rest of the fly is female with normal bristles and red eye-color. The X-chromosomes of each part are shown in the circles. This mosaic is due to the loss of one X-chromosome, containing the dominant genes *W* and *F*, at a later stage than in *A* (probably at a late cleavage division), so that a small portion of the fly is formed of cells with only one X-chromosome, containing the recessive genes *w* and *f*.

cases show that a long series of developmental processes may intervene between the direct effect of a particular gene on the cell which contains it and the visible characteristic of the organism by which we detect this effect.

There may be great differences in this respect between different kinds of organisms. A striking example is the difference between insects and vertebrates in the development of secondary sexual characters. In Drosophila, if one X-chromosome is eliminated during development of a female, all those parts containing a single X-chromosome show strictly male characteristics in every respect, while the parts containing two Xs are strictly female; such mosaics are called *gynandromorphs* (Fig. 176). All the sexual differences are locally determined by the genes present in each part of the body. Thus large parts of the body may be different in sexual characters from the gonads themselves. Similar gynandromorphs are found in other insects, indicating that local determination of sexual differ-

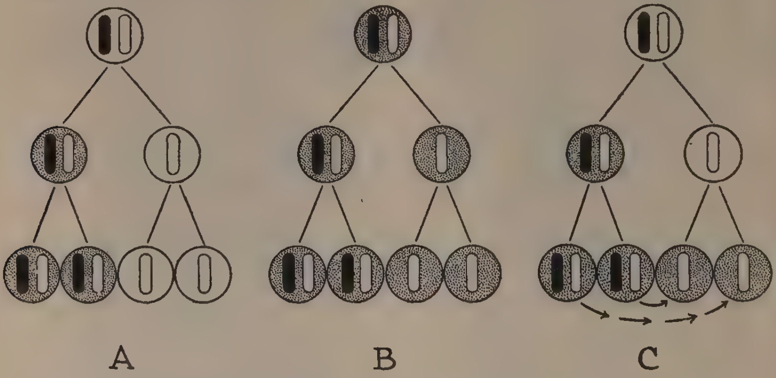


FIG. 177.—Diagrams illustrating differences in the results of chromosome elimination according to the time and place of action of the genes involved. Black rods represent chromosomes carrying the dominant genes, white rods those carrying the recessive allelomorphs; shading represents the phenotypic effects of the dominant genes. In each case the chromosome carrying the dominant gene is supposed to be lost from one cell at the first division shown in the diagram. In *A*, the genes produce their effects after this elimination, and only in those cells where they are present; consequently the organism is visibly mosaic in respect to the characters determined by these genes. In *B*, the effects of the genes have already been produced before the chromosome elimination. In *C*, the effects of the genes are produced after the elimination, but these effects are transmitted in some way (e.g., by internal secretions), as indicated by the arrows, to other cells. In both *B* and *C*, the organism is not mosaic, in appearance, in respect to the characters determined by these genes.

ences is the rule throughout this group of organisms. In the vertebrates, however, the situation is quite different. In these animals many of the secondary sexual differences are determined, largely at least, by internal secretions of the gonads (p. 328). Since the normal mechanism of *inheritance* of sex is essentially the same in the vertebrates as in insects (p. 503), it seems that the sex of the gonads—*i.e.*, whether they are ovaries or testes—must be determined by the genes present in them, and then the internal secretions of these organs secondarily affect the sexual characters of other parts of the body. There seem to be no internal secretions of this kind in insects,

The internal secretions of other ductless glands—thyroid, pituitary, etc.—also have marked effects on development in the vertebrates (p. 327). The genes present in these organs, therefore, indirectly affect many parts of the body. Some hereditary characteristics of vertebrates, however—*e.g.*, eye-color, hair-color, etc.—seem to be strictly locally determined, just as in insects.

Summarizing: genes may produce their visible phenotypic effects either quite directly in the cells where these effects appear, or very indirectly through some mechanism of "remote control" such as the internal secretions of vertebrates. Differences in this respect are found not only between different kinds of organisms but also between different genes in the same organism. Local determination is perhaps more usual in some of the lower animals and in plants than in the vertebrates, but cases of both kinds probably occur in all organisms.

How do the genes produce their effects?—We have seen (p. 529) that, in all cases where there is any evidence on the question, the genes do not produce their effects instantaneously but take an appreciable *time* to do so. This seems to indicate that these effects, even if they occur within a single cell, are produced somewhat indirectly, probably by some specific chemical substances produced by, or under the influence of, the genes and liberated from the nucleus into the cytoplasm. We know that the metabolic processes in cells are governed largely by specific catalysts, called enzymes, produced in the cells, and that the production of these enzymes depends, in many cases at least, on the nucleus (p. 99). There is evidence in a number of cases that the characteristic effects of particular genes are produced through the intermediation of specific enzymes. One such case is that of the "waxy" gene in corn, mentioned above (p. 530). Seeds homozygous for this gene have red-staining starch, while non-waxy seeds have the ordinary blue-staining kind of starch. The red-staining starch probably has smaller molecules than the ordinary kind. In accordance with this, the red-staining starch is more rapidly hydrolyzed by acids or by amylases than the blue-staining kind. It is found, however, that the amylase in the waxy plants is "weaker" than that of non-waxy plants—*i.e.*, the former hydrolyzes starch more slowly than the latter—so that each kind of plant—waxy and non-waxy—hydrolyzes *its own kind* of starch at the same rate. Since the synthesis of starch in the plant is presumably catalyzed by the same enzyme as its hydrolysis (p. 100), these facts strongly suggest that the waxy gene determines, primarily, the kind of amylase formed, which in turn determines the kind of starch synthesized. As the waxy gene produces this effect within a single cell and in a quite short time—*viz.*, in the pollen grain after the reduction division (p. 530)—the production of this specific enzyme seems to be a fairly direct effect of this particular gene.

In other cases in which the method of action of particular genes has been studied, it seems probable that the visible effects are due, directly, to the action of specific catalysts whose production is determined by these particular genes. In most cases, however, it is not possible to establish so direct a relation between the gene and the specific enzyme involved in the end result as in the case of the waxy gene. Indeed, in many cases this relation must be very indirect, as we have seen above (p. 533). Between the primary, direct effect of the gene and the visible or chemically detectable end result there may be a long series of reactions, each resulting in the production of some specific substance which in turn takes part, as catalyst or otherwise, in the next reaction of the series, and so on. In some cases it is possible to disentangle this complex series of reactions, to a certain extent, by means of the effects of temperature or other environmental factors on some of them, by the localization of some of them in particular parts of the organism, or by the interaction of some of the intermediate effects of several genes on a common end result.

On the fundamental problem of how the genes produce their primary effects we have, at present, no direct evidence. The outstanding fact in this connection is that the genes are not "used up" in the process, for every gene is, normally, self-perpetuating, whatever else it may do. If the genes produce their effects on development by influencing some chemical processes in the cells—as seems probable from the facts cited above—they must, therefore, act as *catalysts* (p. 94). The one property which we definitely know all genes to possess—which is, indeed, absolutely essential to their being genes—is that of self-increase, *i.e.*, growth and multiplication, or, in chemical terminology, *autocatalysis*. We do not know the mechanism of this process, but we may conceive it as being somewhat similar to the growth of a crystal (*e.g.*, of salt) in a solution containing its component ions; *i.e.*, the original molecule determines the deposition of more of its component ions, in the same proportions and the same specific spatial relations, about or alongside itself. We do not know what particular feature of composition or structure common to all genes is responsible for this autocatalytic property. We do know, however, that each gene at least doubles itself, on the average, between each two successive cell divisions (p. 516). This action may be represented as a hypothetical chemical reaction, thus:

$$G + A + B + C + \dots \rightarrow 2G + D + E + F + \dots,$$

G representing the gene, A, B, C, . . . all the substances in the cell which furnish the materials for its autocatalytic synthesis, and D, E, F, . . . the by-products of this reaction. In such a system, if one or more of the reacting substances be changed we may expect one or more of the products to be different in consequence. Specifically, if we have a different gene g instead of G we may expect one or more of the by-products of its autocatalysis to be different. Some of these by-products may take part, as catalysts or otherwise, in subsequent reactions in the cell, initiating or modifying a chain of reactions which may therefore differ according to what particular gene catalyzed the original reaction; and the end result of this chain of reactions is what we recognize as the phenotypic effect of this particular gene. On this view, all the effects of the genes—which include, in the final analysis, all the structures and activities of organisms—might be regarded as incidental by-products of the genes' own autocatalytic syntheses. There are other possible ways in which the genes may affect the reaction system of the cell: they may catalyze other reactions independently of their own autocatalysis; they may "over-reproduce" themselves, discharging the excess gene-substance into the cytoplasm, etc.; but these questions can not be decided on the basis of our present knowledge.

Since every gene of the organism is present (normally) in every one of its cells, we may logically suppose that every gene has some effect on the metabolism of every cell, whether or not this effect leads to any result which we can observe. For every gene must be more or less constantly removing certain substances—those furnishing the material for its own growth—from the surrounding protoplasm, and also very probably producing other substances as by-products of this process. In a system of complexly inter-related reactions, such as a living cell, every such removal or addition is very likely to have some effect. We may therefore conceive every gene as producing some effect in every cell of the body and at every stage of development. The effects of certain genes, however, may well be—as we know, in fact, that they are—much more conspicuous in certain parts of the organism than in others, because of differences in the composition of the system—*i.e.*, the cytoplasm—on which they are acting. For instance, if one of the effects of a particular gene is to modify some pigment (*e.g.*, that of the eyes), this effect can be produced only in cells containing this pigment or some substance involved in its formation. As the production of a pigment, or any other component of an organism, involves many reactions, the end result may be, and is, affected by many different genes, which may act in quite different ways and at different stages of the process. Also, each gene may produce several or many different effects in different parts of the organism, depending on the substances present and the processes going on in the cells of each part. The effect of any particular gene in any particular cell depends not only on the nature of the gene but also on that of the cell, which is determined by the effects of all the other genes acting in it, by environmental factors affecting it, and by the antecedent composition and structure of its cytoplasm.

Effects of the external environment.—A developing organism is not an isolated system, but has many complex interrelations with its surroundings. Oxygen, water, and (at least in the later stages of development) other food substances must be supplied to it from outside; waste products of metabolism must be removed; temperature, osmotic pressure, and other physical and chemical conditions must be maintained within certain limits compatible with its life and development. All these factors, collectively, constitute the effective *external environment* of the developing organism. The environmental conditions of development differ considerably, of course, for different organisms. Each kind of organism develops normally under a particular set of environmental conditions. Any considerable departure of any one of these conditions from what is normal for this particular organism may result in more or less extensive abnormalities of development. Beyond certain limits of environmental variation—differing, of course, with different organisms—development ceases entirely or becomes so abnormal that the organism is unable to survive to maturity. The external environment, then, may be said to exert two kinds of effects on developing organisms: a *selective* effect, determining what *kinds* of organisms (*i.e.*, what genotypes) can develop at all in a particular environment; and a *modifying* effect, determining, within certain, usually rather narrow, limits, *how* they develop. We are here concerned chiefly with the modifying effects of the environment; its selective effects will be considered more fully in another place (Chapter XXV).

Temperature is one of the most universal environmental factors affecting development. Some organisms can develop at temperatures as low as 0° C. or even a little lower, while others can develop at temperatures as high as 60° C.; but for most organisms the range of temperatures within which development is possible is much narrower than this, differing considerably for different kinds of organisms. The most general effect of temperature is on the *rate* of development, this effect being similar to that on most chemical reactions (p. 95); *i.e.*, the rate of development is usually increased from 2 to 4 times by a rise of 10° C. (up to the point where further temperature increase becomes injurious). This is additional evidence that many of the processes involved in development are chemical reactions. But the various reactions occurring simultaneously in a developing organism may be accelerated to different extents by the same temperature change. The most favorable temperature for the development of any particular organism is therefore that at which the various developmental processes proceed at rates which harmonize with each other so as to produce normal development. Any considerable change of temperature from the normal range may throw some of the developmental processes out of step with each other, resulting in abnormalities of development. When these abnormalities become too extreme, development ceases and the organism dies. There are other possible ways in which temperature may affect a developing organism, but its effects are probably chiefly due to this differential acceleration of developmental processes. In many cases the end results of temperature differences during development are similar to those of genetic differences; *i.e.*, an individual of one genetic constitution raised at one temperature resembles, phenotypically, an individual of different genetic constitution raised at a different temperature. This is not surprising, on the view that genes act as catalysts, since catalysts and temperature changes both act in essentially the same way, *i.e.*, by modifying the *rates* of reactions (p. 95).

Oxygen and *water* are necessary for practically all organisms at every stage of development. In the absence of certain minimum amounts (which differ considerably for different kinds of organisms) development ceases entirely; above the necessary minimum amounts quantitative variations in the supply of these substances may modify development in various ways.

Food (aside from oxygen and water) is usually derived, during the early stages of development, from the reserve food material stored in the egg-cell (p. 401). After this is used up, however, food materials must be derived, in one way or another, from the external environment. The food requirements of different kinds of organisms differ greatly, of course, and those of the same organism at different stages of development may also differ qualitatively as well as quantitatively. It is obvious that each organism must obtain the requisite amounts of all the food substances necessary for the synthesis of the various components of all its tissues, as well as to meet its energy requirements during development, if it is to develop normally. A quantitative deficiency in food may result merely in retarding development. But it can seldom happen that all the various food substances required will be deficient to exactly the same relative extent. A deficiency will usually involve chiefly one or a few of them. In such cases, those particular organs or processes which are especially dependent on the deficient substances will suffer most, and development may consequently be modified in various ways. The *relative* amounts of various substances in the food supply, above the absolute minimum of each necessary for any development, are therefore important modifying factors in development. Especially in plants, the differences in growth and form occasioned by differences in the ratios of various elements in the food supply are often very striking.

Many other environmental factors—*e.g.*, *light*, *osmotic pressure*, relative concentrations of various *ions*, effects of *parasites*, etc.—may modify development in various ways, or prevent it entirely. The effects discussed above are sufficient to emphasize the general principle that every organism, and every characteristic of an organism, must be regarded as a product of the interaction of genetic and environmental factors during its development, and that the effects of environmental factors may often be quite indistinguishable, except by breeding experiments, from those of genetic factors.

Rôle of the cytoplasm.—Most of the visible processes of development, as well as many of the chemical reactions underlying them, take place in the cytoplasm of the cells. The rôle of the cytoplasm in these processes can not be regarded as a purely passive one, since its composition and structure at each particular stage of development and in each particular cell of the body determine, to a considerable extent, the processes occurring then and there (p. 539). But the characteristics of the cytoplasm itself at any stage are very largely determined by the effects of the genes and of environmental factors at previous stages. There is no beginning of this chain of causes and effects, for each organism consists, at the beginning of its individual existence, of a particular kind of cytoplasm derived from its parents (or, at least, from its mother), in addition to its genes. The fact that, with few exceptions, the hereditary characteristics of the organism are determined entirely by the genes in its chromosomes suggests that the characteristics of the original cytoplasm can not be very important determinative factors in development. There are, however, several ways in which this original cytoplasm does play an important rôle in determining the course and results of development.

In a few cases, as we have seen (p. 509), the cytoplasm contains self-perpetuating, hereditarily transmitted factors which play the same kind of rôle in development as the chromosomal genes. The rarity of cases of cytoplasmic inheritance, however, indicates that it is exceptional rather than usual. The reason for this is evident: even if some of the components of the cytoplasm have the power of specific autocatalysis, or self-multiplication, there is no mechanism for their regular transmission from cell to cell, such as the mitotic mechanism provides for the chromosomal genes; such cytoplasmic components could not, therefore, act as regularly transmitted hereditary factors. Even in the cases of plastid factors, which are the only well-established cases of cytoplasmic inheritance, the transmission is by no means regular (p. 510).

We have seen also (p. 526) that the original cytoplasm of the egg-cell plays an important part in determining the early stages of development, and in a few cases these early effects may determine some characteristics of the adult organism. In almost all cases, however, these maternal effects are entirely overcome by the organism's own genes long before the adult stage is reached. The *F2* generation, whenever it can be obtained, also proves conclusively that the original characteristics of the egg cytoplasm are determined by the genes present in it before reduction and fertilization. The cytoplasm must, then, be regarded as a plastic material, continually modified and made over by the genes affecting it from within, on the one hand, and the environment affecting it from without, on the other hand. In this respect it stands in sharp contrast to the genes, which exhibit a very high degree of stability and self-determination, being usually unmodified by their environment—*i.e.*, the cytoplasm—*provided they are able to live in that environment at all.*

One essential function of the egg cytoplasm is to provide a medium in which the genes can live and grow. No one has yet succeeded in getting a sperm-nucleus to grow or divide in any medium except the cytoplasm of an egg-cell, although a piece of the egg cytoplasm with a sperm-nucleus but no egg-nucleus can develop into a normal, or nearly normal, embryo. The sperm-nucleus, moreover, can not function normally in the cytoplasm of *any* egg-cell, but only in one of the same or a closely related species. In some cases the sperm enters and activates the egg of a distantly related species, initiating development of the egg, but there is no true fertilization—fusion of egg and sperm nuclei—and the sperm takes no further part in the development (p. 419). This is really a kind of "artificial parthenogenesis," the embryo developing with only the chromosomes of the egg-nucleus and, of course, resembling the maternal species in every respect. In some other cases of crosses between different species, the sperm-nucleus fuses with the egg-nucleus, but at the first cleavage division, or sometimes at later divisions, some or all of the paternal chromosomes fail to divide normally and are eliminated from the nuclei. These facts show that the genes, or at least some of them, are able to live and function normally only in cytoplasm of a rather specific kind. What the effective differences between the cytoplasms of different species may be, or why the genes are unable to live and multiply in the foreign cytoplasm, we have as yet no idea. This relation between the genes and the cytoplasm may perhaps be compared to the relation between parasitic organisms and their hosts: many parasites are able to live only in one particular species, or a few closely related species, of organisms—but just why, we do not know.

The mechanism of differentiation.—The most striking feature of development, in all the higher organisms, is the progressive *differentiation* of the various organs and tissues of the body as development proceeds. The method of division and distribution of the chromosomes in mitosis indicates that all the genes of the individual are, normally, present in every cell of the body (except, of course, the mature germ cells), and all the facts of heredity and development substantiate this. The development of all parts of the body must therefore take place under the influence of the same set of genes. The different effects of the genes in different cells must be due to differences in the other components of the cells—*i.e.*, in the cytoplasm—rather than in the genes themselves. The question then is: how do these differences originate? This problem of the *mechanism of differentiation* has been studied more extensively than any other problem of development, and is even yet far from being completely solved. The available evidence, however, permits a general answer to the problem: the initial local differentiations within the egg-cell are due to the effects of certain external environmental factors upon it, either before or after fertilization, and the further differentiations occurring during development are due to effects of different parts of the embryo on each other. These general principles may be illustrated by a brief description of the chief steps in differentiation of the egg and embryo of the frog.[1]

The frog's egg before fertilization is already visibly differentiated into an upper, black (pigmented) hemisphere and a lower, white (unpigmented) hemisphere. The nucleus lies in the upper hemisphere, near the top, while the yolk is confined chiefly to the lower hemisphere; the position of the egg in the water is due to the fact that the yolk is heavier than the other components. The polar bodies are formed at the center of the surface of the black hemisphere; this point is called the *pole* of the egg, and the diametrically opposite point is called the *antipole*. The line through the egg from pole to antipole is called the *primary axis* of the egg. This type of differentiation, called *polarity*, is characteristic of the unfertilized eggs of most animals. Its most constant external manifestation is the formation of the polar bodies at the pole; internally, it is indicated by the position of the nucleus, which usually lies near the pole, and often also by the distribution of yolk, pigment, or other formed bodies in the cytoplasm. It has been shown in a number of animals, and is probably true in all, that the primary polarity of the egg-cell is determined by its topographical relations in the ovary during its formation; *e.g.*, by its point of attachment or of food-supply. This primary differentiation within the egg-cell is thus referable to an environmental factor external to the egg-cell itself. The polarity of the egg has a definite relation to its later developmental differentiation, for the polar hemisphere always forms the *ectoderm*, and the antipolar hemisphere the *endoderm;* eventually the polar region becomes the *anterior end* of the embryo, and the antipolar region its *posterior end.* That these later structural differentiations are actually determined by the differential distribution of substances within the egg-cell is shown by artificially turning and keeping the frog's egg upside-down or sidewise: the redistribution of materials within the cell, due to their different densities, causes the embryo to develop in an abnormal position with reference to the original axis.

---

[1] The experiments on which this account is based have been performed on various kinds of Amphibia, and there are some differences in details between the different species. In particular, the transplantation experiments described in this section (p. 547) have been done chiefly on newts (Triton), and these results may not apply exactly, just as they are stated here, to the frog, but the differences are merely in the *time* relations between invisible (chemical) and visible differentiation (p. 553).

The frog's egg before fertilization is *radially symmetrical* about its primary axis; *i.e.*, *any* plane passing through this axis divides the egg into two identical halves. This symmetry is altered by the entrance of the sperm. The sperm may enter the egg at any point of the polar hemisphere; its entrance initiates movements in the egg cytoplasm which are localized and oriented according to the *point of entrance* of the sperm, and which effect changes in the distribution of substances in the egg. The external manifestation of this redistribution is the appearance of a *gray crescent* at the edge of the black hemisphere on the side directly opposite the point of entrance of the sperm. This redistribution of cytoplasmic substances at the time of fertilization has a determinative relation to the later structural differentiation of the embryo, for the region of the gray crescent becomes the *dorsal side* of the embryo, while the opposite side of the egg becomes the *ventral side*. The egg after fertilization has two axes: the primary axis from pole to antipole, which becomes the longitudinal axis of the embryo, and the *secondary axis* from the middle of the gray crescent to the diametrically opposite point, which becomes the dorso-ventral axis of the embryo. The egg is now *bilaterally symmetrical; i.e.*, it can be divided into two identical halves by only one plane, that passing through both the primary and the secondary axes. This plane of symmetry becomes the *median plane* of the embryo, dividing it into right and left halves. The primary differentiations of the organism, into anterior and posterior ends, dorsal and ventral sides, are thus determined by two external—we might almost say "accidental"—factors: the position of the egg-cell in the ovary, and the point of entrance of the sperm.

These local differentiations become manifest during the cleavage divisions as differences in the *size* and *rate of division* of the cells. The cells of the black hemisphere are always smaller and divide more rapidly than those of the white hemisphere. Within the black hemisphere, also, the cells in the region of the gray crescent are smaller and divide more rapidly than the others. Gastrulation is effected chiefly by the rapidly dividing cells of the upper hemisphere growing downward over the outside of the white hemisphere, which is pushed inward into the blastocoel. The cells of the gray crescent region form the *dorsal lip of the blastopore*, which plays the greatest part in this process of overgrowth. As this overgrowth proceeds, the cells originally at the edge of the black hemisphere are turned under the cells advancing behind them, and thus come to line the enteron in front of the blastopore. The cells of the gray crescent thus become the dorsal wall of the enteron, which later forms the notochord and mesoderm. The ectodermal cells immediately above them—*i.e.*, along the mid-dorsal line of the outer surface—form the neural groove and neural folds, which develop into the central nervous system; the remainder of the outer surface develops into epidermis (and parts of the sense organs), while the cells forming the original lateral and ventral walls of the enteron become the endoderm. If, however, during the stage of gastrulation, a group of cells is *transplanted* from almost any part of the embryo to a different region of the same or another embryo, these cells subsequently develop into the structures normal for the region to which they have been transplanted, regardless of their own original location. In other words, the subsequent differentiation of these cells has not yet been determined at this stage, but is determined later by their location in the embryo. The one exception to this is the *dorsal lip of the blastopore, i.e.*, the region of the gray crescent. If this lip, or a part of it, be transplanted to a different region of the same or another embryo, it nevertheless goes on developing just as it would in its original location; moreover, the subsequent localization of the other

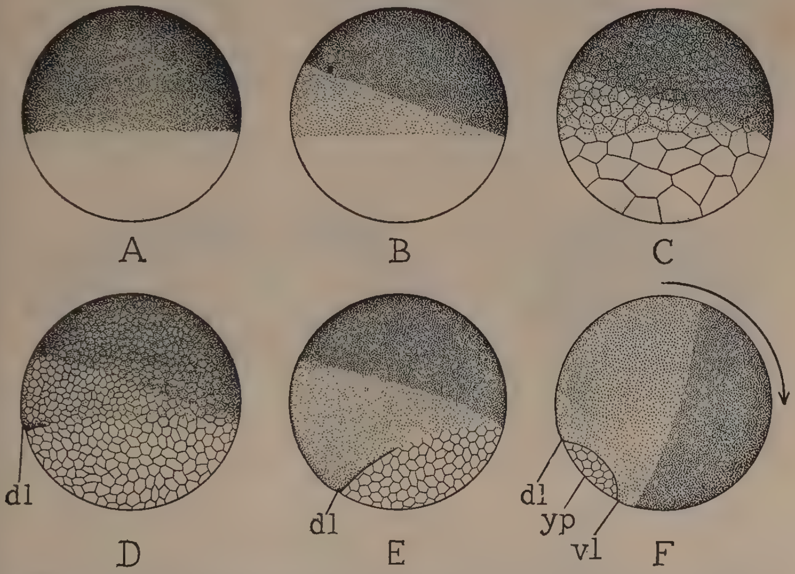


FIG. 178.—Early development of the frog. *A*, unfertilized egg; primary axis vertical, with pole at the top and antipole at the bottom. *B*, after fertilization and appearance of the gray crescent; secondary axis horizontal, with gray crescent at the left; median plane in the plane of the page. *C*, blastula; cells above smaller than those below, those at the left smaller than those at the right. *D–F*, gastrulation; during gastrulation the whole embryo rotates as indicated by the arrow, so that the primary axis, originally vertical, becomes the longitudinal axis, with the pole at the anterior end, and the secondary axis, originally horizontal, becomes the dorso-ventral axis, with the original gray crescent region on the dorsal side. *dl*, dorsal lip of the blastopore; *vl*, ventral lip of the blastopore; *yp*, yolk plug. (Cf. Fig. 133.)

parts of the embryo is determined by this transplanted dorsal lip. At this stage, therefore, the dorsal lip of the blastopore seems to control the development of the whole embryo; this region is therefore called the *organizer* of the embryo. The "organizing" power of this region can be traced even further back; for if the gray crescent region of the egg be destroyed or removed during or before cleavage, at any time after the gray crescent has appeared, the remainder of the egg will never form anything but a ball of cells; while if any other region be destroyed or removed, the part containing the gray crescent will nevertheless develop into a normal (or approximately normal) embryo. It seems, then, that the early local differentiation of the egg (before and just after fertilization) determines primarily the location of the gray crescent region, which subsequently determines the location of all other parts of the embryo. Just after the "organizing" region of the dorsal lip has been invaginated to form the dorsal wall of the enteron, all the other regions of the embryo are still *undetermined:* a piece from any part of the surface transplanted to the mid-dorsal line, just above the organizer, will develop into the nerve-cord. A short time later, however, although no *visible*

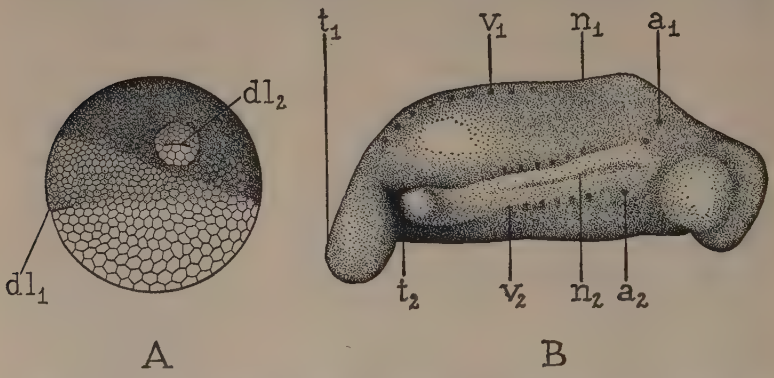


FIG. 179.—*A*, an embryo at the beginning of gastrulation, into which has been transplanted, in the position shown, an organizer from another embryo of the same stage; dl_1, original dorsal lip; dl_2, transplanted dorsal lip. *B*, the same embryo at a later stage; t_1, v_1, n_1, a_1, tail, vertebra, neural tube, and auditory vesicle, in their normal positions, developed under the influence of the original organizer (dl_1); t_2, v_2, n_2, a_2, tail, vertebra, neural tube, and auditory vesicle of the secondary embryo, developed under the influence of the transplanted organizer (dl_2). (Adapted from Spemann.)

differentiation has yet occurred in this region, the surface ectoderm above the organizer has become *determined*, and will now develop into a nerve-cord wherever it may be transplanted. At this time other regions of the embryo, further away from the organizer, are still undetermined. If a piece of the mid-dorsal region, after it has become determined, be transplanted to another region of the embryo, it will determine not only its own subsequent visible differentiation, but also that of other parts in its vicinity, acting as a *secondary organizer*. As development proceeds each part of the embryo in succession becomes determined, under the influence of the primary or secondary organizers, before its visible structural differentiation begins. This "invisible" determination (proved by transplantation experiments) must depend on some chemical differentiation within the cells, which precedes and determines their subsequent visible differentiation. Each part, once it has become determined, is *self-differentiating—i.e.*, it proceeds along its own special line of development, into certain particular tissues and organs, more or less independently of other parts of the embryo—and may also act as a secondary organizer on other still undetermined parts.

These facts raise the questions: *what* is localized in the "organizing" regions, and *how* do they exert their influence on other parts of the embryo? These questions can not yet be answered with certainty, but there is some evidence bearing on them. We have seen (p. 546) that the first visible manifestation of the regional differentiation of the developing embryo is the different *rate* of cell division in different parts. It has been found, in many kinds of organisms, that regional differences in rate of cell division are accompanied or preceded by differences in rate of metabolic processes, as manifested by oxygen consumption, CO_2 production, etc. In general, the region of highest metabolic rate is the pole of an egg, the anterior end of an animal, or the growing point of a plant. From this point the rate decreases progressively, backward or downward, so that there is a *gradient* of metabolic rate along the axis of the organism. This metabolic gradient is accompanied by a gradient of *electrical potential*, the regions of higher metabolic rate having a more *negative* potential than those of lower rate, just as an excited region of a nerve (or any other tissue) has a more negative potential than an unexcited region (p. 239). There is also a gradient of rate of cell division, coinciding with the metabolic and electrical gradient. If the metabolic gradient be upset, by subjecting the region of high rate to poisons or anaesthetics temporarily, the subsequent development may be abnormal, especially with respect to the relative size of the parts.

We have learned (in Chapter VI) that the rates of metabolic processes are determined chiefly by catalysts, or enzymes, in the cells. The differences in metabolic rates in different parts of an organism, or even of a single cell (*e.g.*, an egg-cell), therefore indicate differences in concentration of some catalytic substance or substances. We have learned, moreover, that what we call "metabolism" is a complex of many intricately interrelated chemical reactions, each catalyzed by different enzymes. What we call "metabolic rate," as measured by oxygen consumption, CO_2 production, or any such external manifestation, is only a very crude measure of the "lump sum" of many—not necessarily all—of these intracellular reactions, and tells us little or nothing about the nature or *relative* rates of the different reactions. It has been explained previously (p. 100) how the concentrations of specific catalysts may determine not only the velocity but also the end results of metabolic processes, by differentially accelerating different reactions which are "competing" for the same food substances. The differences of metabolism in different parts of a developing organism, manifested externally as gradients of metabolic rate, almost certainly involve also differences in the nature of the metabolic processes, determined by the differential distribution of various specific catalysts within the organism, as we know, in fact, to be true in the adult multicellular organism (Chapter XII).

In the unfertilized egg (*e.g.*, of the frog) there is a metabolic gradient along the primary axis, due to some previous external factor in the ovary, such as the proximity of blood-vessels from which the oocyte receives its food and oxygen supply (p. 545). The region of highest metabolic rate is the pole of the egg, which, as we have seen, always (normally) becomes the head end of the embryo. The entrance of the sperm initiates movements in the egg cytoplasm and a redistribution of some of its components, resulting in a new region of high metabolic rate—the region of the gray crescent—which sets up another gradient along the secondary axis. There are now two metabolic gradients in the egg, at right angles to each other. The location of each point in the egg with reference to these two gradients—its latitude and longitude, so to speak—determine the rate and, as explained above, the nature of the metabolic processes at that particular point, which, in turn, determines *what will develop there*. The region of highest metabolic rate, between and including the pole and the gray crescent, will develop into the structures of the mid-dorsal line (notochord and central nervous system), the first parts of the embryo to differentiate; the region of lowest rate, on the opposite side of the egg, will become endoderm; etc.

The fate of each part of the egg is, however, as we have seen (p. 547), not necessarily fixed at this stage. It seems, rather, that the region of highest metabolic and developmental rate—the gray crescent region—determines not only its own development but also that of the other parts of the embryo. If this "organizing" region be transplanted to any other part of an embryo, it seems to set up a new gradient, overcoming the original gradients of the rest of the egg. Its ability to do this, however, decreases progressively as development proceeds and the various parts of the embryo successively become "set"; it also varies greatly in different kinds of eggs at the same stage of visible development (p. 553). But *how* is this "control" effected, or, in more general terms, how does one part of the embryo influence the development of other parts? There are several mechanisms by which such effects may be—and in some cases are known to be—exerted. These mechanisms may be classified as (1) mechanical, (2) chemical, (3) electrical, (4) radiant.

(1) There are many examples of *mechanical* effects of one part of an embryo on other parts. If the two cells of a frog embryo after the first cleavage division be separated, each may develop into a *whole* embryo (p. 554); but if one of these two cells be killed and left attached to the other, the remaining cell develops into a *half* embryo; this difference

must be due to a purely mechanical effect of the dead cell on the living one. The distribution of the inert yolk material in eggs seems to play a large part in determining the form of the cleavage divisions (p. 395); this effect is undoubtedly, to a large extent, a purely mechanical one. The form of gastrulation in the frog's egg seems to be largely a mechanical effect of the more rapid growth of the cells of the upper hemisphere, especially those of the dorsal (gray crescent) side. Other changes in form, such as the formation of the neural tube, the elongation of the embryo in its longitudinal axis, etc., must also be largely mechanical effects of unequal rates of growth in different parts; these changes of form must necessarily exert mechanical effects on the subsequent development—at least in external form—of other parts.

(2) One part of an organism may affect other parts *chemically* either by removing substances from them or by supplying substances to them; both these kinds of effects on developmental processes are definitely known in certain cases (p. 329). The gradients of metabolic rate in developing organisms strongly suggest the *diffusion* of some substance or substances from a region of high concentration to other parts (p. 76). On the other hand, a region of higher metabolic rate may hold down the metabolism of other regions by using up some substance or substances more rapidly, causing a diffusion of such substances *toward* the region of higher rate.

(3) We have noted that there is a gradient of *electrical potential* coinciding with the gradient of metabolic rate, the more active region being electro-negative, as usual in living tissues. We have learned (in Chapter XVI) how a negative potential, or state of excitation, is transmitted from one part of an organism to other parts—what is called *nervous* or *neuroid* transmission. This mechanism, which is the principal method of coordination in organisms in general, probably plays a very important rôle in the regulation of developmental processes also. If an external (*i.e.*, artificial) current be passed through the stem of a plant, placing the positive electrode on the tip of the growing point, so as to reverse the normal potential gradient, the growth of the terminal bud is suppressed, and that of the lateral buds is

accelerated just as when the terminal bud is removed or killed (p. 447). Similar results have been obtained by similar experiments on developing animals. These facts make it seem very probable that the normal potential gradients play an important part in the coordination of developmental processes.

(4) It has recently been found that *dividing* cells emit *radiant energy*, in the form of *ultra-violet* radiation; the mechanism of this process seems to be similar to that of bioluminescence (p. 280). This ultra-violet radiation, moreover, accelerates cell-division in other cells on which it falls. These facts are not yet firmly established; should they prove to be generally true, they may be of great significance in explaining how the most active regions of the developing embryo exert their "organizing" effect on neighboring parts. As cells absorb ultra-violet rays quite strongly, the stimulating effect of the most rapidly dividing cells would be confined to the immediately adjacent regions, and would only slowly be transmitted through the embryo as each region in turn took up the accelerated rate of cell division, thus producing a gradient of developmental rate such as we have seen actually does exist in the embryo.

All these mechanisms may be involved—perhaps to different relative extents in different cases—in the "regulation" of development, *i.e.*, in determining the orderly sequence and coordination of the various developmental processes.

Although the factors involved in developmental differentiation are probably essentially similar in all organisms, there are great differences, among different kinds of organisms, in the *time* relations between the invisible determination (chemical differentiation) of the parts and the visible processes of development, such as cleavage. In some coelenterates each cell of the 16-cell stage will, if isolated, develop into a normal embryo; there has therefore evidently been no differentiation, even invisibly, between the cells up to this stage. In some other animals (*e.g.*, echinoderms), each cell of the 4-cell stage can develop into a normal embryo, but there are fixed differences between the upper (ectodermal) and lower (endodermal) cells of the 8-cell stage. In the frog each cell of the 2-cell stage can usually develop into a whole embryo if isolated, the first cleavage division usually passing through the middle of the gray crescent, so that each of these two cells contains part of the "organizing" region. Sometimes, however, the first cleavage division does not pass through the gray crescent; in this case, if the two cells be isolated, the cell containing the gray crescent can develop into a normal embryo, but the other cell, which contains no organizer, will never develop into anything but a ball of cells. In many animals, as in the frog, the plane of the first cleavage division has no invariable relation to the internal differentiation of the egg except that it always passes through the primary axis. In some animals, however, there is a definite, invariable relation between cleavage and internal differentiation; in such cases the subsequent development of each cell may be already determined even at the 2-cell stage. In most cases the internal differentiation of the egg, except for its primary polarity, takes place *after* fertilization, as in the frog; but in some animals the parts of the egg are already determined, to a considerable extent, before fertilization. The most extreme cases of "pre-determination" in the egg are found among insects. In some insects (*e.g.*, flies), if any part of the egg-cell be destroyed before or immediately after fertilization, all the other parts develop just as they would in the whole egg; *i.e.*, the development of each part is already determined in the egg before fertilization. In these animals the location of all the parts of the embryo in the egg is determined by the position of the egg-cell in the ovary during its formation. All these different types of eggs, however, are alike in that the local differentiations within the egg are determined originally by some external factor or factors.

Respective rôles of genetic and environmental factors.—We have seen that the localization and differentiation of parts during development, within what was originally (in the oogonium) undifferentiated cytoplasm, are determined, in one sense, by environmental factors. But *what kind* of organism the egg, as a whole, develops into, and *what kinds* of tissues and organs each part, once localized, develops into, are determined by its genes. The location of the median plane, of the front and hind ends, of the dorsal and ventral sides, are determined, as we have seen, in the frog's egg, by environmental factors. But that this egg is to develop into a bilaterally symmetrical animal at all (rather than radially symmetrical, like coelenterates and plants), that it is to develop a nervous system on the dorsal side (rather than on the ventral side, as in many invertebrates), that it is to develop a brain and a head at the front end, and that it is finally to become a frog and a particular kind of frog, are all determined by its genes. We might say, very roughly speaking, that the genes determine *what* is to develop, the environmental factors *where* it is to develop. This is well illustrated by experiments in which an organizer is transplanted from one species of frog to the egg of a different species of frog or other amphibian. The location of the organs of this "mixed" embryo is determined by the position of the transplanted organizer, but the specific characteristics of each organ are those of the species from which the cells composing this organ were derived. Such an embryo is essentially similar to a mosaic produced by chromosome elimination (p. 532). The difference between normal, cytoplasmic, differentiation and a mosaic condition in which there are *genetic* differences between different parts —which occurs only as an abnormality—is well illustrated by such a mosaic as that shown in Fig 176, *B*. A part of this fly, comprising one shoulder, front leg, and corner of the head, differs genetically from the rest of the animal, as shown by the forked bristles, male sex-comb, and white eye-facets. The nuclei of all these cells were derived from one nucleus which had accidentally lost one of its *X*-chromosomes. Nevertheless, some of these cells developed into eye tissue, some into shoulder, and some into leg, according to their *position* in the organism. Environmental factors—*i.e.*, effects of the surrounding parts—determined that certain cells should develop into eye tissue, but their own genes determined that this should be *white* eye tissue; environmental factors determined that certain other cells should develop into a leg, but their own genes made this a *male* leg; etc. And, it is important to note, as shown by other evidence, if these cells had lacked *both* *X*-chromosomes (or both chromosomes of any pair) they could not have developed into anything at all, regardless of any effects of surrounding cells or any other environmental factors.

The respective rôles of genetic and environmental factors in development may be summarized, roughly, as follows: The visible processes of development are the results of various chemical reactions among the components of the cells and food substances derived, directly or indirectly, from the external environment. These reactions are determined largely by specific catalysts, or enzymes, produced in the cells. These catalysts are produced, directly or indirectly, by the genes, acting on the various components of the cytoplasm. The differences among species and individuals—genetic differences—are due to differences among their genes; while differentiation *within* the individual is due to differences in the localization of the cytoplasmic substances on which the genes act, these local differences being traceable ultimately to environmental factors.

CHAPTER XXIV

VARIATION AND SELECTION

It is a familiar fact that no two individual organisms are *exactly* alike; the same thing may be said of non-living objects also, if we interpret the word "exactly" sufficiently rigorously. All differences among organisms related by descent are called *variations*. Variations may be classified according to their causes, as follows:

I. *Genetic* variations:

(1) *Recombinations:* genetic differences due to the normal operation of the mechanism of heredity, *i.e.*, segregation, independent assortment, crossing-over, and random fertilization.

(2) *Aberrations:* variations due to occasional irregularities in the behavior of the chromosomes.

(3) *Mutations:* changes in individual genes.

II. *Modifications:* differences due to *environmental* factors, this term including all factors except the genes which may affect an organism in any way.

These several classes of variations can not usually be distinguished by their phenotypic appearance. In general, any characteristic of an organism may be affected in any way and to any extent by any one of these causes of variation or a combination of them. The underlying causative factors, in any particular case, can only be determined by breeding experiments, combined, in some cases (aberrations), with microscopic study of the chromosomes.

Recombinations.—We have learned, in the chapter on heredity, of the mechanisms whereby the genes of a diploid organism are "shuffled" at the maturation of the germ cells and brought together, at fertilization, in various new combinations. Only in case both parents are homozygous for *all* their genes will all their offspring be genetically identical; n all other cases there will be genetic differences among the offspring of the same parents due to different *recombinations* of genes in the gametes produced by the parents and the zygotes resulting from the unions of these gametes.

We have already (pp. 459-483) considered the numbers of different genotypes and phenotypes so produced in some of the simplest cases. We may now generalize and extend these results, as follows: An organism heterozygous for n pairs of genes will produce 2^n genetically different classes of gametes (provided none of these genes are completely linked to each other or so closely linked that there is complete interference [p. 491] among them). If one parent is heterozygous for m pairs of genes and the other for n different pairs, there will be 2^{m+n} different genotypes among their offspring. If both parents are heterozygous for the same n pairs of genes, there will be 3^n different genotypes among their offspring. If none of these genes is completely dominant to its allelomorph, the number of different phenotypes will be equal to that of genotypes. If some of the genes are completely dominant, the number of phenotypes may be less, depending on the nature of the cross, but the "hidden" genotypes will show up as phenotypes in some subsequent generation. In general, then, the number of genetically different types among the offspring increases rapidly with the number of genes for which the parents are heterozygous; in mathematical language, the former is an *exponential function* of the latter.

Under natural conditions of random mating, all individuals, in dioecious or cross-fertilizing organisms, are usually heterozygous for many genes. Under these conditions, therefore, there is usually a large amount of genetic variation, due to recombination of genes, among the offspring of the same parents. In organisms such as man, where the number of offspring of the same parents is relatively small, it can practically never happen that any two of them will be genetically identical (except, of course, identical twins).

We have seen that each part and characteristic of an organism may be affected by several or many different genes. When the parents are heterozygous for a number of genes affecting the same characteristic, there will be many different types among their offspring in respect to this characteristic; this is particularly true of such characteristics as size, vigor, fertility, etc., which are affected, to a greater or less extent, by very many, perhaps most, of the genes. When the number of genetically different classes is large and the differences between them relatively small, the amount of variability within each class (due to non-genetic factors) may be greater than the differences between them, so that the different classes overlap and it becomes impossible to distinguish them by their phenotypic appearance. This situation—the absence of sharply separable classes—is called *continuous variation* (p. 575). Under natural conditions variation due to recombination of genes is more frequently than not of this apparently continuous type, especially in respect to characteristics which are affected by many different genes.

Aberrations.—We have learned, in previous chapters, how remarkably precise is the mechanism whereby the genes are transmitted: the division and distribution of the chromosomes at mitosis and maturation. Indeed, these processes are among the most regular ones in living organisms. As in other natural phenomena, however, this regularity is not absolute: occasionally the machinery "slips a cog," giving rise to unusual groupings or relations of the chromosomes. In many cases the new systems produced by such *aberrations* are thereafter automatically perpetuated by the normal workings of the mechanism.

These chromosomal aberrations may be classified as follows:

(1) Aberrations involving a whole *set* (haploid or diploid) of chromosomes:

haploidy
triploidy
tetraploidy
etc.

(2) Aberrations involving one or more (less than n) *whole chromosomes:*

non-disjunction
elimination
attachment
fragmentation

(3) Aberrations involving *parts* of one or more chromosomes:

deficiency
duplication
translocation
inversion

We shall consider briefly the nature and results of each of these different types of aberrations.

(1) Aberrations involving a whole set of chromosomes may occur by failure of a nucleus to divide after the chromosomes have divided, or by fusion of two nuclei after division. Either of these abnormalities occurring at or after the reduction division will result in *diploid gametes.* Occurring in ordinary diploid cells they will result in *tetraploid* nuclei, containing $4n$ chromosomes; these, if germ cells, will later produce, by normal reduction divisions, diploid gametes. A diploid gamete fertilized by a normal haploid gamete will produce a *triploid* zygote, containing $3n$ chromosomes; but if fertilized by another diploid gamete it will produce a tetraploid ($4n$) zygote. Both triploid and tetraploid individuals have been found in many species of organisms. They are usually larger in all their parts than the normal diploid individuals, and often differ from them slightly in other phenotypic characteristics. The triploid and tetraploid types differ markedly from each other in the production of gametes. The triploid individuals produce, by reduction divisions, gametes having every possible chromosome number from n to $2n$, but those with the intermediate numbers are most frequent. Usually, however, only those gametes with either n or $2n$ chromosomes (or nearly so) are viable; most of those with intermediate numbers die or fail to function. Consequently, triploid individuals are highly sterile; *i.e.*, they produce very few offspring. Tetraploid individuals, however, usually produce only diploid ($2n$) gametes, all of which are viable and functional; consequently these individuals are perfectly fertile. Tetraploid races are found in nature among many plants, but seldom among animals. The reason for this difference is obvious: most plants are monoecious and often self-fertilizing; consequently a tetraploid race, producing both male and female diploid gametes, will perpetuate itself. Most animals, how-

ever, are dioecious; a tetraploid individual if produced will usually, by chance, mate with a diploid one and produce triploid offspring, which are highly sterile; therefore the race soon dies out.

From a tetraploid race, by subsequent aberrations of the same kind, *hexaploid* (*6n*), *octaploid* (*8n*), etc., individuals may be produced. In many plant groups related species have chromosome numbers which are multiples of a common denominator, suggesting that they may have originated in this way from a common ancestor (Fig. 181).

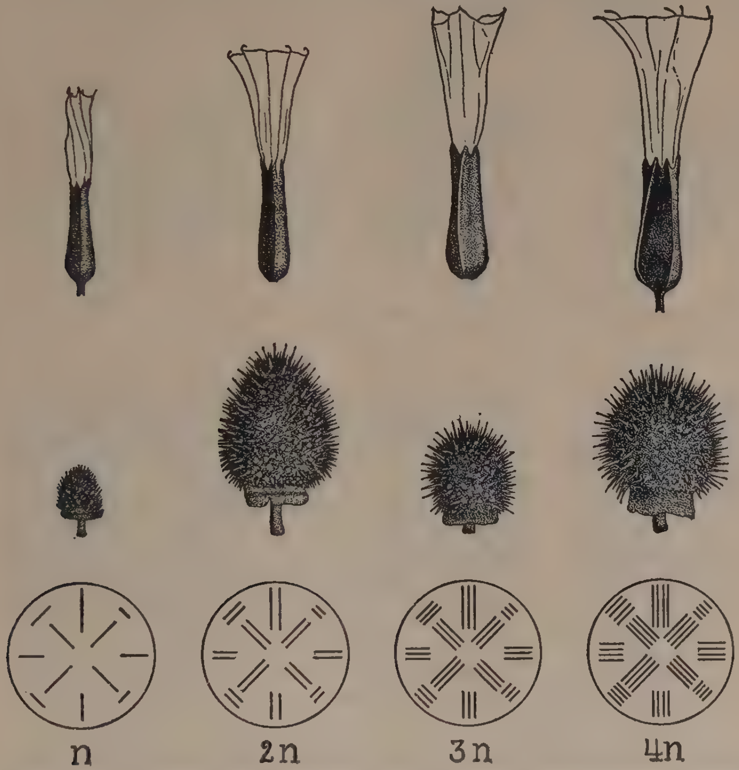
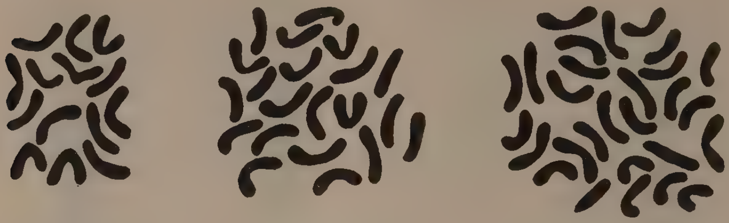
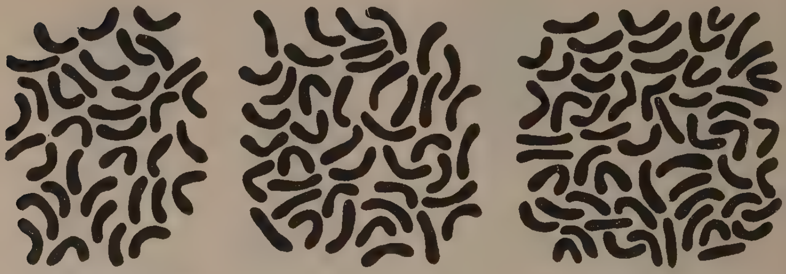


FIG. 180.—Flowers, seed capsules, and chromosome groups of haploid, diploid, triploid, and tetraploid Jimson-weeds (Datura stramonium). The small size of the seed capsules of the haploid and triploid plants is due to the low fertility of these forms, producing relatively few seeds. (Adapted from Blakeslee.)

In Drosophila, triploid females are occasionally found, but no triploid males. A triploid female mated to an ordinary diploid male produces both diploid and triploid offspring, but in relatively small numbers, most of those with intermediate chromosome numbers being inviable. The triploid offspring are of two classes, XXX and XXY, both classes having, of course, three of each of the other chromosomes (autosomes). The XXX triploids are females, scarcely distinguishable phenotypically from ordinary diploid females, and normal in every respect except for their low fertility as explained above. The XXY triploids, however, are *intersexes*, intermediate between males and females and completely sterile. The explanation of this result, put in the simplest terms, is: each X-chromosome contains a gene for "femaleness" which we may call f, but the Y-chromosome does not contain this gene or, so far as we know, any allelomorph of it (p. 498), while each member of one pair of autosomes contains a gene for "maleness" which we may call m. The constitutions of the different



diploid (14) triploid (21) tetraploid (28)



pentaploid (35) hexaploid (42) octaploid (56)

FIG. 181.—Chromosome groups of different species of roses. Some of these forms (those with odd chromosome numbers, at least) are probably hybrids. (After Täckholm.)

classes, in respect to their chromosomes and the genes involved in sex-determination, may be represented thus (A = one haploid set of autosomes):

	Chromosomes	*Genes*
Diploid female.........	$AA\ \ XX$	$mm\ \ ff$
Diploid male..........	$AA\ \ XY$	$mm\ \ f$
Triploid female........	$AAAXXX$	$mmmfff$
Triploid intersex.......	$AAAXXY$	$mmmff$

A ratio of $1\ m : 1\ f$ produces a female, $2\ m : 1\ f$ a male, and $1.5\ m : 1\ f$ an intersex. This shows that sex, like other characters of the organism, is affected by more than one pair of genes; in fact, there may be more than two pairs involved—we have merely given the simplest possible explanation of the facts. Since there are, and can be, no triploid males, the triploid condition can not be perpetuated under natural conditions; artificially, we can maintain a line of triploid females by selecting triploid females in each generation to breed.

In a number of seed-plants, *haploid* individuals (sporophytes) occasionally occur, presumably by an abnormal type of haploid parthenogenesis (p. 450). These individuals are smaller and less vigorous than the normal diploid plants. They are also highly sterile, because most of the gametes formed, by random distribution of the n chromosomes to the two poles at the reduction division, have less than a complete haploid set of chromosomes and are inviable. The few offspring produced, by self-fertilization or by crossing to diploid individuals, are diploid (or, in some cases, with one or two chromosomes less than the full diploid number).

(2) *Non-disjunction* is the failure of chromosomes to disjoin (*i.e.*, separate) normally at a mitotic or a reduction division, resulting in one cell receiving more and the other less than the normal number of chromosomes. Usually only one chromosome is involved. Non-disjunction at a reduction division therefore results in gametes containing $n+1$ and $n-1$ chromosomes; at an ordinary diploid mitosis, in cells with $2n+1$ and $2n-1$ chromosomes, which, if germ cells, will later produce some $n+1$ and $n-1$ gametes. Chromosome *elimination* is the loss of a chromosome, usually due to its lagging on the spindle and failing to be

included in either daughter nucleus. This aberration results in cells with $2n-1$ chromosomes and gametes with $n-1$ chromosomes.

Gametes with $n+1$ or $n-1$ chromosomes, fertilized by normal gametes, produce zygotes with $2n+1$ or $2n-1$ chromosomes. In some cases these offspring are viable, but they usually differ more strikingly from the normal $2n$ individuals than haploid (n), triploid ($3n$), or tetraploid ($4n$) individuals do. This is due to the fact that the *balance* of the different genes, carried in different chromosomes, is upset by the loss or gain of a single chromosome more than it is by the addition or subtraction of one or more whole haploid sets. In Drosophila, individuals with a missing or an extra *Y*-chromosome or *IV*-chromosome are viable, those with an extra *X*-chromosome are sometimes viable but always very weak and sterile, those with a missing or an extra *II*- or *III*-chromosome are never viable. In a number of other organisms, chiefly plants, forms are known with $2n-1$ or $2n+1$ chromosomes. The $2n+1$ forms are, quite generally, less abnormal and more viable than the $2n-1$ forms. Besides their phenotypic differences from

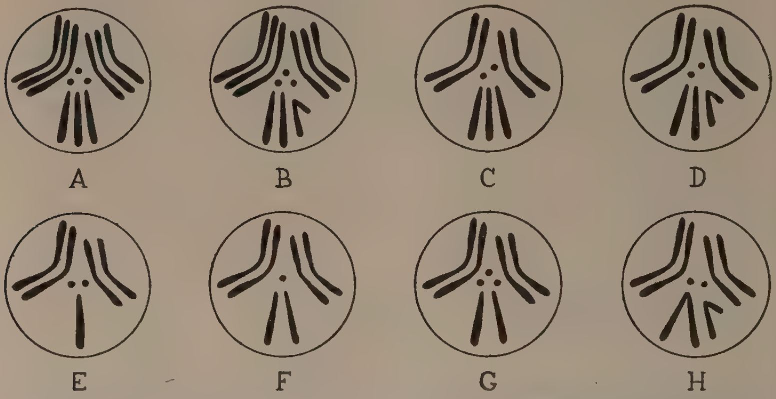


FIG. 182.—Abnormal chromosome groups of Drosophila melanogaster (the normal chromosome groups are shown in Figs. 166 and 167). *A*, triploid female; *B*, triploid intersex; *C*, triplo-X female; *D*, XXY female; *E*, XO male (no Y-chromosome); *F*, haplo-IV (only one IV-chromosome); *G*, triplo-IV; *H*, attached-X female (these always have a Y-chromosome, as shown, receiving the two attached X-chromosomes from their mother and a Y from their father; the sons of these females receive the Y from their mother and an X from their father, thus reversing the normal sex-linked inheritance).

the normal forms, they also give unusual results in heredity, due to the peculiarities of their reduction divisions occasioned by the extra or missing chromosomes. By union of two $n+1$ gametes, or of two $n-1$ gametes, zygotes with $2n+2$ or $2n-2$ chromosomes may be formed; but these forms are usually inviable, the $2n-2$ ones probably always so because of the entire lack of the genes located in the missing pair of chromosomes.

Non-disjunction or chromosome elimination may occur in somatic as well as in germ cells, resulting in *mosaics*, as explained in the preceding chapter (p. 532).

In some cases two chromosomes become permanently *attached* to each other. In other cases one chromosome may *fragment* into two or more separate ones. These aberrations result in changes in the total number of separate chromosomes, and also in the linkage relations of the genes in these chromosomes. In Drosophila, for instance, there are races in which the two X-chromosomes are permanently attached to each other, giving an unusual type of sex-linked inheritance. These changes are automatically perpetuated, once they have occurred. They produce no phenotypic changes, since the number of each kind of genes is unaltered, and are only detected by the unusual linkage relations in heredity or by microscopic study of the chromosomes. In many groups of organisms, the relations of number, size, and shape between the chromosome groups of related species suggest that they may have originated by such aberrations from a common ancestor.

(3) *Deficiency* is the loss of a part of a chromosome. It usually produces marked phenotypic effects, as well as irregularities of heredity. Individuals homozygous for the deficient chromosome are usually inviable, due to the entire lack of the genes located in the missing portion, while those heterozygous for it (having one deficient chromosome and one normal homologous chromosome) show more or less marked phenotypic effects, due to changes in the normal balance of different kinds of genes.

Duplication is the presence of a part of a chromosome in an abnormal location *in addition to* being present in its normal location. The phenotypic effects are usually less marked than those of a deficiency, but the duplication is apparent by irregularities in heredity, such as abnormal linkage relations of the genes in the duplicated section of chromosome.

Translocation is the presence of a part of a chromosome in an abnormal location *instead of* its normal location; *i.e.*, the removal of a piece from one chromosome and its attachment to another chromosome. This shows no phenotypic effects so long as the individual is "balanced," *i.e.*, contains both the deficient chromosome and the one with the translocated piece attached to it, but the translocation is apparent by irregularities in heredity, such as abnormal linkage relations. When these two chromosomes become separated, by segregation and independent assortment, some of the offspring, of course, have a deficiency and others a duplication.

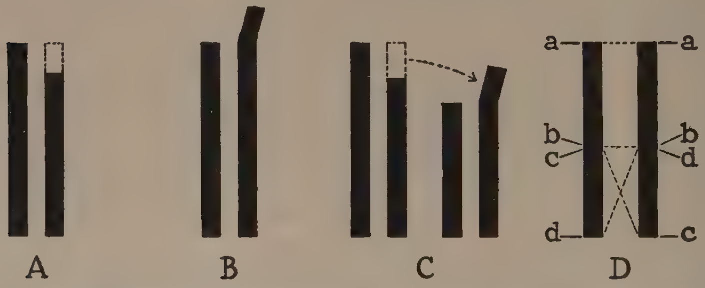


FIG. 183.—Diagrams illustrating sectional aberrations. In each case the normal chromosome is shown on the left, the abnormal one on the right. *A*, deficiency; *B*, duplication; *C*, translocation; *D*, inversion.

Inversion is the turning end for end of a section of a chromosome within the same chromosome. This has no phenotypic effects, but is manifested by unusual linkage relations of the genes in the inverted section.

Cases of all these types of sectional aberrations are known in Drosophila, and some of them in other organisms also. In at least one case, two closely related species differ from each other by inversion of a section in one pair of chromosomes. Some other species seem to differ by translocations of portions of chromosomes. We do not yet know much about how any of these conditions originate. Probably some of them are due to abnormalities of synapsis and crossing-over. It has recently been found that such aberrations can be produced by X-ray treatment, even in the "resting" stage—*e.g.*, in mature sperms—so that they do not necessarily occur at mitosis or maturation.

Mutations are changes in single genes. Such changes are often difficult, in practice, to distinguish from some of the types of chromosome aberrations described above, especially those involving only short sections of chromosomes containing but a few genes. For this reason, all such changes are often included in the term mutation; but this term will be restricted here to changes in single genes, *i.e.*, changes of the genes themselves rather than of the machinery of their distribution.

A mutation results in the production of a different gene at the locus of the gene which has mutated. The new gene behaves, in heredity, as an allelomorph of the original gene present at the corresponding locus of the homologous chromosome. The new gene is commonly called a *mutant* gene, and the original one its *normal allelomorph;* there is no distinction, however, between a "normal" and a "mutant" gene except that the latter is known to have originated, by mutation, from the former. A change in a single gene is impossible to detect by microscopic observation of the chromosomes. The occurrence of mutation is detected by the phenotypic effects of the mutant gene as contrasted with those of its normal allelomorph. Mutations may be classified, roughly, according to the extent of their phenotypic effects, as:

(1) *slight* mutations, whose effects are not readily detectable without special methods of study, such as accurately measuring large numbers of individuals, enhancing the effects of the mutant gene by means of other genetic or environmental factors which affect the same character, etc.;

(2) *visible* mutations, whose effects are readily detectable visually, *i.e.*, by a difference in the appearance of the individuals containing the mutant gene sufficient to distinguish them sharply from otherwise identical individuals containing its normal allelomorph;

(3) *lethal* mutations, whose effects are so great as to kill the individuals containing the mutant gene before they reach maturity.

In many cases a mutant gene which produces a very slight (scarcely detectable) effect when heterozygous, produces a marked visible effect or even a lethal effect when homozygous; in such cases the mutant gene is called *recessive.* In other cases, a mutant gene produces an easily visible effect when heterozygous and a lethal effect when homozygous; in these cases the mutant gene would be called *dominant* in respect to its visible effect, but recessive in respect to its lethal effect. The terms dominant and recessive, as previously emphasized (p. 469), are purely relative. In general, the terms *slight*, *visible*, and *lethal* mutations are to be understood as referring to the effect of the mutant gene when homozygous.

Mutations are, on the whole, rare occurrences. Generally speaking, genes are extremely stable; *i.e.*, they reproduce themselves and are transmitted from cell to cell for generation after generation without change. The very existence of hereditary resemblance among related organisms depends, as has been previously emphasized (p. 515), on this relatively great stability of the hereditary factors. In Drosophila melanogaster, it has been estimated, very roughly, that about one individual in 50,000 shows a new mutation of the visible type. Lethal mutations have been found (in a series of experiments especially designed to detect them) to be about six times as frequent as those of the visible type. The reason for this greater frequency of lethal mutations is obvious: an organism is a very complex and delicate piece of machinery; a mutation effects a random change in this machine, comparable to "throwing a monkey wrench into the machinery," and such a change is much more apt, on chance, to injure the machine than not—indeed, the most probable result is to wreck it. The greater the change produced, the more likely it is to be injurious or even fatal; in fact, most mutations of the visible type are more or less deleterious to the organism, while those of the slight type may have little or no injurious effect. We have no way of estimating, even roughly, the frequency of slight mutations, as most of them escape detection entirely, but there is reason to believe that they are more frequent, perhaps much more frequent, than the visible ones. There is no reason to suppose that mutations are either more or less frequent in Drosophila than in other organisms: in this species at least 25,000,000 individuals of known genetic constitution have been examined by observers competent to detect visible mutations when they occur, and some 500 such mutations have been found; it is very likely that under the same conditions a comparable number would be found in any other kind of organisms.

There are great differences in the frequency of mutation of different genes. Of the estimated 2,000–3,000 different genes in Drosophila, not more than about 400 have produced visible mutations which have been detected, and most of these have done so only once. Some of them, however, have mutated (giving visible changes) twice, three times, etc., up to 25 times in the case of one locus, all these recurrences of mutation in the same locus being independent of each other. There are also a number of cases, in several species of plants and animals, of very mutable genes, which mutate as frequently as several or many times in each individual (in different cells, of course); these cases are, however, quite exceptional.

A mutant gene necessarily behaves in heredity as an allelomorph of the original gene from which it arose, since it occupies the same locus in a homologous chromosome. So far as we know, there is no way in which different allelomorphs at corresponding loci in homologous chromosomes can have originated except by mutation at some time in the past. In Drosophila, practically all the visible mutants have originated in pedigreed cultures under observation, so that we know in each case which is the mutant and which the original allelomorph: *e.g.*, the gene *w*, determining white eye-color (p. 502), originated by mutation from its allelomorph *W;* the gene *b*, determining black body-color (p. 479), from its allelomorph *B;* etc. In wild races of organisms, and also in many cultivated races whose history is unknown, it is impossible to tell which allelomorph is the original and which the mutant one, or whether both of them may have arisen by mutations, at different times, from a still different original gene at the same locus. Not only the differences between races or varieties of the same species, but also the differences between species and between larger groups of organisms are of the same kinds as the changes produced by mutations; but species usually, and larger groups always, differ by many such differences. So far as we know, *all* genetic differences among organisms (except such as are due to chromosome aberrations) are due to mutations at some time in the past.

The same gene may mutate in several different ways, *i.e.*, give rise to several different mutant allelomorphs. For instance, the gene *W* (the normal allelomorph of "white") in Drosophila has given rise, at different times, to eleven different mutant genes, each having a different effect on eye-color (and some of them, at least, having other phenotypic effects also); some of these mutations have recurred several times independently. Any two of these genes behave in heredity as allelomorphs of each other, though only two of them, of course, can be present in the same individual (except in triploid or tetraploid individuals). Mutant genes are, in general, neither more nor less stable than the original ones; *i.e.*, they mutate, on the average, about as frequently. In the series of "white" allelomorphs, several of the mutant genes have given rise to other mutant allelomorphs and also to the normal allelomorph: *e.g.*, the gene w^e ("eosin") has arisen by mutation both from *w* ("white") and from *W* ("red"), and has also mutated both to *w* and to *W; W* has mutated to *w* several times, as well as to w^e and to other allelomorphs; etc. The same kinds of relations are also found at other loci in this and other organisms. It is a fairly general rule (though not without exceptions) that different mutations at any one locus affect chiefly the same part or characteristic of the organism, though in different ways and to different extents. This fact suggests that some of the phenotypic differences of the mutant from the original type may, in many cases, be due to the alteration of the normal effect of the original gene rather than to any positive effect of the mutant gene. It is even possible that some mutations may be simply a complete loss of the normal gene; but this can not be generally true, as shown by the fact that mutant genes often give rise to different mutant genes and even to the normal allelomorph again.

Mutation may occur in any kind of cell and at any stage of development. If a mutation occurs in a germ cell, its effects will appear in the offspring or in subsequent descendants (if the mutant gene is recessive, its phenotypic effects may not appear in the first generation). If a mutation occurs in a somatic cell, its effects may appear in those parts of the body derived from this cell, producing a *mosaic* —an individual with genetic differences between different parts of its body (p. 532). Mosaics due to mutation are found, however, only in cases where the mutant gene is dominant (produces a visible effect when heterozygous) or is in the *X*-chromosome of a male (in which case it has no allelomorph, since the *Y*-chromosome is mostly "empty"). This fact shows that mutation occurs in only one allelomorph of a pair, even when the two allelomorphs are identical. The distribution of the differences among the parts of such mosaic individuals also shows that mutation occurs in only one cell of the individual, all the cells containing the mutant gene being derived from this one (except in the cases of very mutable genes, in which mutation may occur frequently in each individual, producing mosaics which are a veritable patchwork). If a mutation occurs in a cell which subsequently gives rise to both somatic and germ cells, its effects may appear both in part of the body of this individual and in some of its offspring; such cases are fairly frequent in plants, where the meristem cells of each growing point give rise to all the somatic tissues of that particular branch and also to the germ cells, both male and female, of the flowers on that branch (p. 448). It is thus often possible, in plants, to preserve a mutation first appearing as a mosaic, by breeding from the flowers on that part of the plant where it appears.

As to the nature and cause of mutation we have known, until very recently, practically nothing. Mutations apparently occur in all organisms, though usually quite rarely. Some genes are more liable to mutate than others, but we have no idea why. Only one gene mutates at a time, even when it is one of two identical genes in the same nucleus. The change, whatever its nature, seems to be sudden and complete, the new gene being, in general, just as stable as the original one from the moment the mutation has occurred. There is no evidence (except in a few cases of exceptional, very mutable genes) that the frequency of mutation of any particular gene is affected by other genes in the organism; pure races produce mutations just as frequently as hybrids. Until very recently, no environmental factor had been found to affect the rate of mutation markedly; mutations occur under natural as well as artificial conditions.

Within the last few years, two kinds of physical agencies have been found to increase the frequency of mutation markedly, and these results promise to throw some light on the nature and cause of mutations. The first of these agencies is *temperature.* It has been found, in Drosophila, that individuals kept at a higher temperature produce more mutations, the frequency of mutation being increased about three times by an increase of 10° C. in temperature. Such great effects of relatively small temperature differences are characteristic of the rates of most *chemical* changes, while processes of a non-chemical nature are usually affected very much less by temperature differences (p. 95). This may be considered as a strong indication, at least, that mutation is a chemical change. Indeed, it had long been supposed that a mutation is a chemical change in the gene, chiefly because it was difficult to imagine what else it might be; but the demonstration of the large temperature effect furnishes a somewhat more secure basis for this hypothesis.

The most striking success in increasing the number of mutations has been obtained by subjecting the cells to *X-rays.* The frequency of mutations, in Drosophila, has been increased about 150 times by this method, and similar results have been obtained in other animals and in plants. The same results are obtained whether the gametes, zygotes, immature stages, or adults are X-rayed. The kinds of mutations, the relative frequency of the various kinds (p. 568), and the relative mutability of different genes are the same as under natural conditions; *i.e.*, all kinds of mutations are increased in the same proportion. The X-ray results further confirm several conclusions previously drawn: that mutation may occur at any stage of development; that it may occur during the "resting" (*i.e.*, non-dividing) stage of the nucleus, as for instance in mature sperm-cells and in dormant seeds, and therefore seems to have no relation to mitosis or maturation; that only one gene mutates at a time and that it mutates completely, strengthening the hypothesis that the gene ordinarily consists of a single molecule, or at least not of several or many molecules of the same kind.

The only other agency which has been found to have an effect on the frequency of mutation comparable to that of X-rays is *radium radiation*, which is very similar in nature to X-rays. It is known that these very short-wave radiations are able to knock electrons loose from atoms or molecules, and that these free electrons can bring about further chemical changes in molecules which they happen to strike. There are always some stray short-wave radiations and free electrons in nature—from radioactive elements and other sources—and the possibility is suggested that all mutations may be due to this cause; *i.e.*, that a mutation is a chemical change in a gene which happens to be hit by a short-wave radiation or a free electron. This is not yet proved—but it is the only suggestion we have at present as to the nature and cause of mutations.

Modifications.—Even among genetically identical individuals, there are always some individual differences. These variations due to non-genetic factors are called *modifications*. All non-genetic factors capable of modifying or affecting an organism in any way are called *environmental* factors. Environmental factors affect the organism at every stage of its existence: the gametes before fertilization, the embryo while still within the parent (in mammals, seed-plants, etc.), as well as the free-living immature and adult stages. We have discussed, in the preceding chapter (p. 539), some of the ways in which environmental factors may affect and modify the development of organisms. Adult organisms also may be modified in various ways by their environment. Such modifications may be produced not only by the direct effects of environmental factors (temperature, nutrition, etc.) on the organism, but also indirectly, through the effects of the organism's own responses to its environment; *e.g.*, the development of muscles by use, the development of conditioned reflexes by training, etc.

Environmental factors may, like genetic factors, affect practically any characteristic of an organism in any way and to any extent. In general, those characteristics of an organism which are most liable to genetic variation (*i.e.*, are markedly affected by many different genes) are also most readily modified by environmental factors. Just as with the effects of mutations, the greater the modification the more likely it is to be injurious, so that there is always a limit to the extent to which an organism can be modified in any particular respect without killing it. In general, plants are more capable of extreme modification by environmental factors than animals, and lower animals more than higher animals: the more complex the machine, the less it can be modified without wrecking it.

Since the same characteristics of an organism may be affected, and often in the same ways, by environmental as by genetic factors (p. 540), it is, in general, not possible to distinguish modifications from genetic variations by inspection. An organism of one genetic constitution, under one set of environmental conditions, may be similar in appearance to an individual of different genetic constitution under different conditions; *e.g.*, an individual with genes for large size may be stunted by starvation to the same size as a well-fed individual with genes for small size. To properly test the effects of environmental factors, we must start with individuals that are genetically identical; and conversely, to test the effects of genetic factors we must submit all individuals to as nearly as possible the same environmental conditions throughout their development.

There is, however, one absolutely distinctive difference between variations due to genetic and those due to environmental factors: the latter *are not inherited*. In former years, before the mechanism of heredity was understood, there was much dispute over the question whether environmental modifications—"acquired characters," as they were called—could be inherited. Thousands of experiments have been performed to answer this question, and the results of all these experiments are quite conclusive: such variations are never inherited. A few cases which, from time to time, have been supposed to show such inheritance have always been subsequently proved to be due to faulty experimental methods or uncritical interpretation of the results. The question is now no longer a disputable one, as our present knowledge of the mechanism of heredity shows the inheritance of environmental modifications to be impossible. In making this statement, it must of course be clearly understood that we do not include in the term "environmental modifications" such *genetic* changes as gene mutations and chromosome aberrations, which may also be due, directly or indirectly, to environmental factors. To be inherited, a change must affect either the genes themselves or the mechanism of their distribution, *in the germ cells.* While our knowledge of the causes of these genetic changes is still very incomplete (p. 573), we know certainly that they are not caused by most of the ordinary environmental factors which modify the somatic characteristics of organisms. It might be supposed that environmental factors which may affect the cytoplasm of the germ cells (nutrition, disease, etc.) might cause heritable changes, but in fact any such effects, provided they are not fatal, are quite temporary, usually not persisting beyond the early embryonic stages and never reappearing in the next generation. In practice, therefore, it is always possible to distinguish between genetic and environmental variations by breeding from the somatically different individuals and determining whether the differences reappear in their offspring all raised under the same environmental conditions.

While it is possible to get a race or line of individuals all of which are genetically identical—*i.e.*, to eliminate genetic variation entirely (except for the rare occurrence of aberrations or mutations)—it is never possible to control all environmental factors so exactly as to eliminate *all* environmental variation. Even among genetically identical individuals raised under the most uniform possible environmental conditions, there is always a certain residual amount of individual variation, ascribable to uncontrollable slight environmental differences affecting the organisms at every stage of development. Among the practically uncontrollable environmental differences are those affecting the gametes (especially the egg-cells) and the embryos while still within or attached to the parent; *e.g.*, differences of location in or on the parent, resulting in differences of nutrition.

Continuous variation; statistical methods.—It has been noted above (p. 559) that, in the case of characters which are affected by many different genes, the many classes representing the various possible recombinations of these genes are often not sharply separable by inspection, and the variation consequently appears *continuous; i.e.*, there is a continuous series of gradations from one extreme to the other, *e.g.*, from the smallest to the largest, or from the lightest to the darkest, individuals. This is also generally true of environmental variations, for these are usually due to many different environmental factors each exerting some effect, in one direction or another, on the variable characteristic. In most mixed populations (groups of individuals selected at random) under natural conditions both these causes of variation are operative; consequently the variation among such organisms is usually, in respect to most characters, of the apparently continuous type. It should be clearly understood that what we call continuous variation is always due to multiplicity of factors—genetic or environmental or both—affecting the character in question; the more we can simplify the conditions, experimentally, the more clearly does all variation appear *discontinuous*, *i.e.*, consisting of definite, sharp differences between groups of individuals.

In many cases it is not possible or convenient to simplify the conditions sufficiently to resolve the apparently continuous variation into its several components, and methods have been devised for studying such variations in bulk, so to speak. These methods, especially devised for the elucidation of variations affected by a multiplicity of factors, are called *statistical* methods. Statistical methods can only be applied to quantitative variations, *i.e.*, to characters which can be measured or counted. Characters which can not be accurately measured (*e.g.*, color), however, can be treated quasi-statistically by classifying them into a number of grades (*e.g.*, from lightest to darkest), assigning to each grade an arbitrary number (1, 2, 3, 4, etc.), and treating these differences as though they were measured quantities.

The statistical method of studying continuous variation —*e.g.*, in the size of organisms or of particular parts of organisms—begins by dividing all the individuals into a number of classes, based on the unit of measurement employed; *e.g.*, if we are measuring the lengths of beans in millimeters all those beans between 9 and 10 mm. are one class, those between 10 and 11 mm. the next class, etc. (Fig. 184). All the class intervals must be equal, in terms of the unit of measurement; in the example given, the class interval is 1 mm., and this same unit must be maintained throughout the whole series, from the smallest to the largest beans,

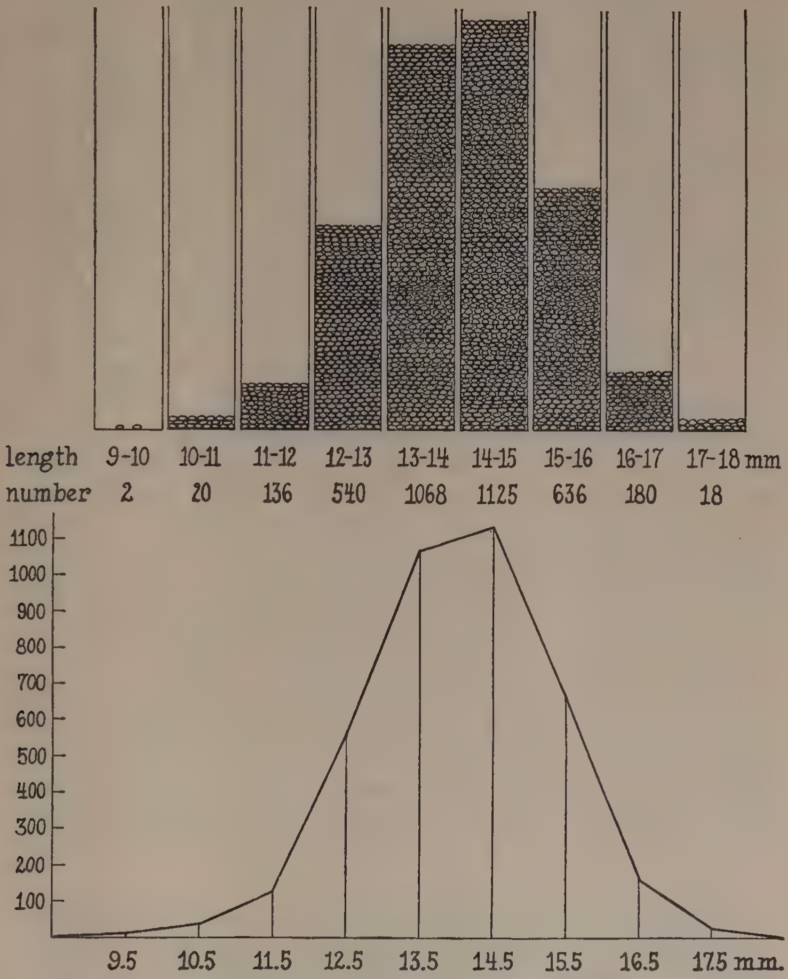


FIG. 184.—Above: 3,725 beans classified according to length. Below: frequency distribution curve of the same beans; abscissae, lengths in millimeters; ordinates, number of beans in each class. The ordinates are erected at the midpoint of each class interval; i.e., all beans in the 14–15 mm. class are counted as 14.5 mm. long, etc. (Adapted from Johannsen.)

regardless of how many or how few individuals fall in each class. The class interval should also, if possible, be so chosen that all the individuals are divided into at least 8 or 10 classes, preferably more. The next step is to record the number of individuals in each class; this is called the *frequency-distribution.* This distribution may be represented graphically by means of a curve whose abscissae are the magnitudes of the variable characteristic in the respective classes (*e.g.*, lengths in mm. in the example given), and whose ordinates are the frequencies, *i.e.*, numbers of individuals in each class (Fig. 184). Such frequency-distribution curves have various forms in different cases, but there is one form which is approximated in a great many cases of continuous variation: the form known as the *normal curve* or *curve of probability* (Fig. 185). In general, the larger the number of factors affecting the results, and the more nearly equal the influences of these various factors, the nearer will the frequency-distribution approach the normal curve. This curve shows graphically the facts that: the greatest number of individuals is in the middle (*median*) class; the distribution is symmetrical on both sides of this largest (*modal*) class; the frequencies diminish, at first slowly and then more rapidly, as the differences from the modal class increase in either direction, but a small number of individuals (if the total number be large) may differ from the modal value by very large amounts. The actual frequency-distributions obtained, in various cases, may differ from this normal distribution in various ways: the curve may be asymmetrical ("lopsided"), it may have two or more modes ("humps") instead of one, it may be flattened at the top or curtailed at the ends, etc.

The characteristics of any particular frequency-distribution may be expressed by means of a number of figures called the *statistics* of this particular distribution. The most important of these is the *mean*, or average value of the whole population (*i.e.*, of all the individuals measured). If the distribution is normal, this coincides with the *mode*, or most frequent value; but in other types of distribution it may not. The second important statistic of any distribution is a measure of the *dispersion*, or variability, of the population. In the distribution curve, this is shown by the relative width of the curve (as a whole) in terms of the unit of measure employed: if the population is very variable, the curve will be spread out widely; if it is less variable, all the individuals will be clustered more closely about the mean value. Other statistics of a frequency-distribution express its degree of skewness ("lopsidedness"), of flatness at the top, etc.

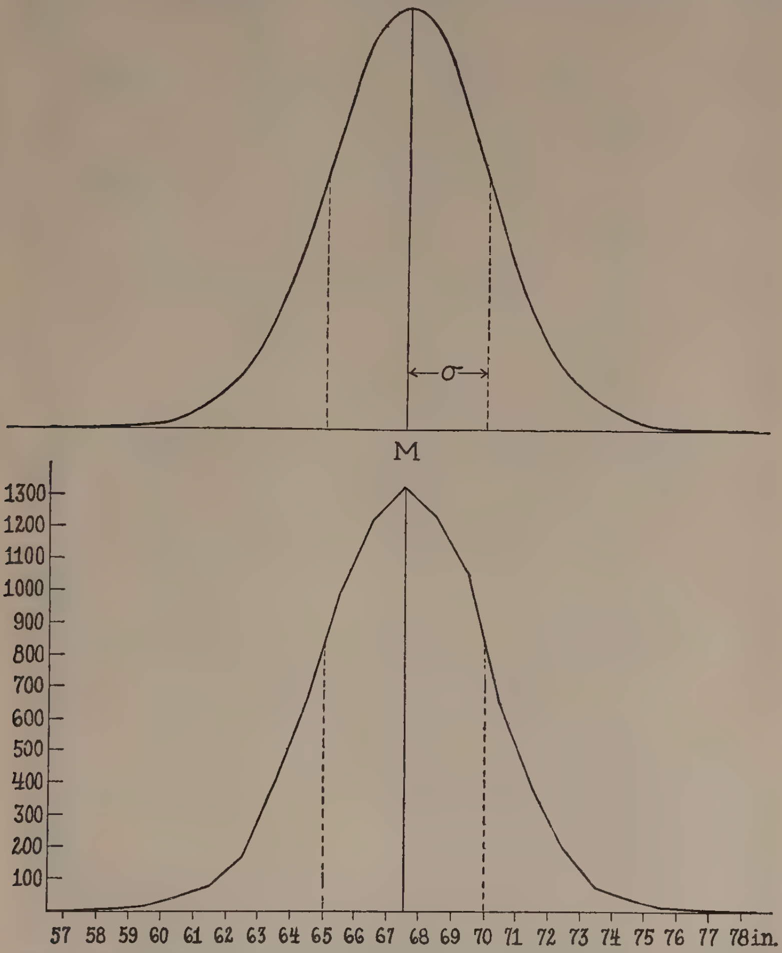


Fig. 185.—Above: the theoretical normal curve; *M*, mean; σ, standard deviation (distance from the mean to point of inflection of the curve), the usual measure of dispersion. Below: frequency distribution curve of heights of 8,585 men; $M = 67.46$ inches; $\sigma = 2.57$ inches. (Adapted from Yule.)

Statistical methods enable us to express in concise terms, which can be handled mathematically, certain significant features of otherwise unwieldy masses of measurements of variable quantities. As variability is characteristic of all phenomena, statistical methods are employed in all fields of science. They are widely used in fields, such as those of human affairs, where experimental methods are impossible or inconvenient. In general, however, their greatest utility is in connection with, and supplementary to, experimental methods; rarely can statistical methods alone furnish reliable information as to the causes of, or the fundamental relations among, observed phenomena. In the study of variability among organisms, statistical methods are employed chiefly for the comparison of different populations (groups of individuals) to determine whether or not there are any real differences between them. In some cases these methods may also give some indication of the probable causes of such differences; *e.g.*, statistical comparison of the frequency-distributions of different groups of offspring with those of their parents may furnish a rough estimate of what proportion of the total variability is due to heredity.

In general, variability due entirely to environmental factors will *usually* tend to give an approximately normal frequency-distribution. The same type of distribution is often found in cases of genetic variability, when the same characteristic is affected by many different genes with more of less equal effects. When the differences are determined chiefly by one pair, or a very few pairs, of genes, but to a lesser degree by other genetic or environmental factors, the frequency-distribution may be a continuous curve with two or several distinct modes; *i.e.*, the population consists of two or several distinct classes which overlap to some extent. Accurate analysis of any variable group of organisms into its component classes, and determination of the causative factors of the variations, can only be effected by experimental breeding.

Selection.—From any variable group of organisms we may *select* for breeding, in each generation, those showing a particular characteristic or combination of characteristics, or, in cases of continuous variation, those showing a particular characteristic in its most extreme form, *e.g.*, the largest or the smallest individuals. The results of such selective breeding will differ according to the nature of the original population and the breeding methods employed. Any group of organisms of the same species, picked at random under natural conditions, constitutes a *mixed population.* The individuals composing such a population usually show considerable variation, due partly to genetic and partly to environmental differences; their frequency-distribution in respect to any particular characteristic—*e.g.*, size—often approximates the normal curve. The results of selection—*e.g.*, for large size—in such a population differ considerably in the cases of *self-fertilizing* and *cross-fertilizing* organisms. Many plants—peas, beans, oats, barley, wheat, etc.—are normally self-fertilizing. In these plants pollination and fertilization of the egg-cells occur before the flowers open, so that there is very little chance for cross-fertilization under natural conditions, although this can be effected artificially by removing the stamens before the pollen is ripe and later cross-pollinating these flowers. In many other monoecious plants, however, cross-fertilization is the rule, especially in plants with large, showy flowers, which are usually cross-pollinated by insects; such plants often have special mechanisms which prevent self-pollination under natural conditions, although this can be effected artificially. All *dioecious* organisms, whether plants or animals, are of course necessarily always cross-fertilizing.

We shall consider first the effects of selection in a self-fertilizing species, as this is the simpler case. For this purpose, we may consider the effects of selection for size among beans. Starting with a mixed population of beans of one species—*i.e.*, a number of beans picked at random from many plants of this species—we may select and plant the smallest beans and the largest ones. The offspring of each of these individual beans will be variable in size, but *less variable* than the original population. Moreover, the *average* size of the offspring of the largest beans will, in general, be *larger* than the average size of the original mixed population; and the average size of the offspring of the smallest beans will be *smaller* than that of the original population. Selection, therefore, has effected, in each case, a change in the *mean* (average) size and also in the amount of

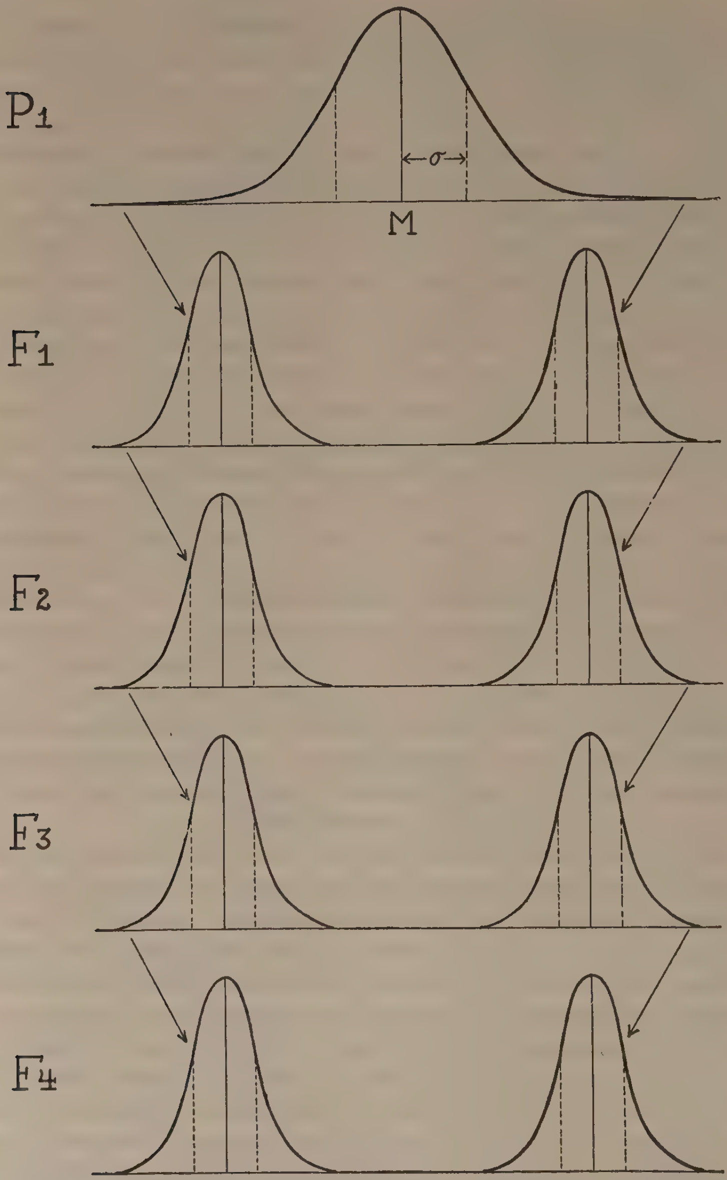


FIG. 186.—Diagram illustrating the effects of selection in a self-fertilizing organism. The first line represents the frequency distribution of the original mixed population; *M*, mean; σ, standard deviation. The following lines represent the frequency distributions of subsequent generations bred from the smallest individuals (on the left) and the largest individuals (on the right) in each generation. In this case, the effect of selection is the isolation of two pure lines in the F1 generation, and subsequent selection has no further effect.

variability. Now let us select again, from among the offspring of each original bean, the largest and the smallest individuals, keeping the different lines separate. In the next generation, we find that the average size and the variability of the beans on each plant are the *same* as those of its parent plant, and that there is no difference between the offspring of the largest bean and those of the smallest bean *from the same plant.* In other words, selection is effective only among the individuals of a mixed population, *not* among the progeny of any one individual. This result is always (or almost always) obtained when we are dealing with a self-fertilizing species. The explanation of this result is simply that in such a species each individual is, ordinarily, *homozygous* for *all* its genes, because all its ancestors for many generations have been self-fertilized. The only ways in which an individual of such a species can become heterozygous are by a mutation or by an accidental cross-fertilization—both rather rare occurrences. Even when such an event does occur, the offspring of the heterozygous individual tend to become all homozygous again in a few generations of self-fertilization, because each heterozygous individual produces, in each generation, both heterozygous and homozygous offspring, while each homozygous individual produces only offspring like itself (p. 459). For these reasons, almost any individual of a self-fertilizing species, picked at random, is homozygous for all its genes. All the offspring of such an individual, by self-fertilization, will therefore contain exactly the same set of genes, and all the variations among these offspring are due entirely to environmental factors. Since such variations are not inherited, selection among these offspring is entirely without effect; so long as the environmental conditions remain similar, the mean size, range of variation, and in fact the entire frequency-distribution will remain the same throughout successive generations, regardless of which individuals are selected to breed from. The same things hold true for any other variable characteristic as well as for size. A group of organisms all descended from a single homozygous individual by an unbroken series of self-fertilizations is called a *pure line.* Within a pure line selective breeding is entirely without effect, unless a mutation *happens* to occur affecting the particular characteristic for which we are selecting; the process of selection, however, in no way increases the probability of such a "lucky" mutation. When a mutation does occur, the continuance of self-fertilization tends to separate the progeny of the heterozygous individuals, within a few generations, into two pure lines, one identical with the original pure line and the other homozygous for the new gene.

Another situation similar, in many respects, to a pure line is that of organisms propagated entirely by asexual methods. In most asexual methods of reproduction—budding, cuttings, grafting, polyembryony, etc., and diploid parthenogenesis without reduction or chromosome elimination—all the offspring are genetically identical with the parent (p. 507). Under these circumstances, also, selection is entirely without effect. A group of organisms all descended from a single original individual by exclusively asexual reproduction is called a *clone*. A clone differs from a pure line in that the individuals comprising a clone may all be heterozygous for one or more pairs of genes if the original ancestor was; so long as asexual propagation is continued, there is no segregation or reassortment of these genes, but if any one of these individuals reproduces sexually (whether by self- or cross-fertilization) the various possible genetic recombinations will appear in its offspring (p. 558). Many cultivated plants—fruit trees, ornamental shrubs and trees, garden flowers, potatoes, etc.—are propagated commercially by exclusively asexual methods—cuttings, grafting, bulbs, tubers, etc.—in order to secure uniform progeny free of genetic variations (p. 508).

In plants or animals which are normally cross-fertilizing (whether monoecious or dioecious), the results of continued selection in successive generations are quite different from those described above. If we start, again, with a mixed population and select for some particular characteristic—*e.g.*, size—we obtain, again, in the first generation offspring, a decrease in the amount of variability and also a change of the mean size in the direction selected for. But, if we now continue to select for the same characteristic among the offspring of each individual (or pair), we obtain further changes of the same kind in the second and subsequent

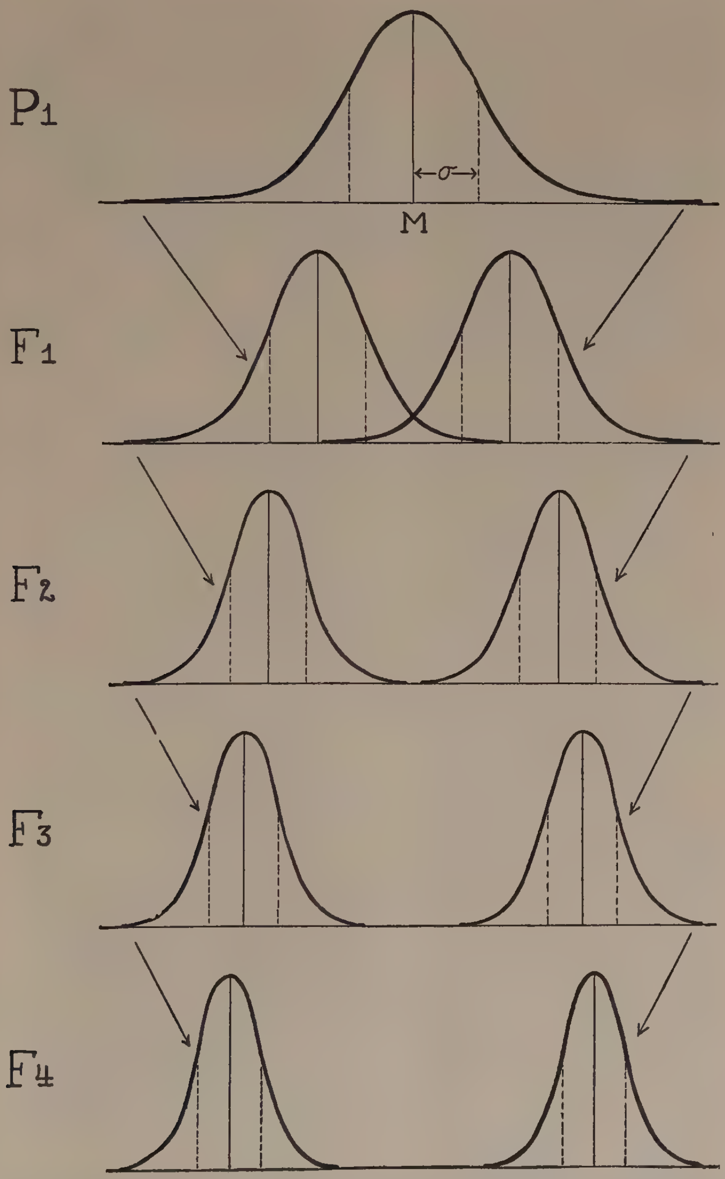


FIG. 187.—Diagram illustrating the effects of selection in a dioecious or normally cross-fertilizing organism; symbolism the same as in Fig. 186. In this case, the effects of continued selection are a gradual shift of the mean in the direction of selection and decrease of the standard deviation (i.e., of the variability), for several generations; but these effects become smaller in each successive generation.

generations. On the average, however, these changes, in both mean size and range of variability, are smaller in each successive generation, and finally, after several generations, selection has no further effect. The difference between this result and that obtained with self-fertilizing organisms is due to the fact that in a cross-fertilizing species each individual is, ordinarily, heterozygous for many pairs of genes, because all its ancestors for many generations have been cross-mating at random. Random mating in a mixed population tends to distribute all the different genes throughout the population; almost any individual of such a population, picked at random, is therefore heterozygous for many pairs of genes. The offspring of such an individual will therefore exhibit many genetic variations, representing the various possible recombinations of these genes (p. 558). By selecting for some one characteristic—*e.g.*, large size—in successive generations we gradually accumulate in the selected line all those genes of the original ancestors which favor large size, and eliminate all those which favor small size. By this process we finally get a line which is homozygous for all genes affecting size; after this, selection has no further effect, unless a mutation favoring large size *happens* to occur in the selected line. The same things hold true for any other variable characteristic as well as for size. A selected line, obtained in this way, is equivalent to a pure line so far as concerns those particular characteristics for which it has been selected.

True pure lines can be produced artificially in monoecious plants, such as corn, which are normally cross-pollinated. Such plants can, usually, be self-pollinated artificially; by continuing this procedure for a number of consecutive generations, pure lines are produced in which all individuals are genetically identical and homozygous for all their genes. Such artificially established pure lines are similar in every respect to the pure lines of naturally self-fertilizing organisms.

In dioecious organisms, such as most higher animals, it is impossible to produce pure lines in the strict sense of the definition (p. 583), since such organisms can not be self-fertilized. The same result—the production of a line of genetically identical individuals homozygous for all their genes—can, however, be effected by *inbreeding*. Strict inbreeding means mating brother to sister in every generation. Other things being equal, seventeen generations of brother-sister mating are approximately equivalent in effectiveness to six generations of self-fertilization in producing a homozygous line. When complete homozygosis has been obtained by this method, such a line is entirely similar, in respect to variability and selection, to a pure line of self-fertilizing organisms; such inbred lines of animals are therefore often called "pure lines." In practical animal breeding the term inbreeding is commonly applied to the mating of individuals related less closely than brother and sister, *e.g.*, first cousins; such breeding methods gradually increase the proportion of homozygosis, tending toward the condition of a "pure line," but more slowly than strict inbreeding.

One very frequent result of artificial self-fertilization or inbreeding, in naturally cross-fertilizing plants or animals, is a decrease in the general vigor of the inbred line, as compared with the mixed population. Under the term *vigor* we include such characteristics as rate of growth and development, general healthiness and resistance to unfavorable conditions, fertility, etc.—all those general characteristics which favor the survival of the individual and the race under natural conditions. It is popularly supposed that this decrease in vigor is due to inbreeding as such, but this is not true. It is due simply to the accidental accumulation in the inbred line of recessive genes whose effects are more or less deleterious. In a mixed population most of the individuals, as pointed out above, are heterozygous for many genes, and the unfavorable effects of the recessive genes are suppressed by their dominant allelomorphs. Individuals having *dominant* genes whose effects are unfavorable are soon eliminated, under natural conditions, by their inability to compete successfully with more vigorous individuals; consequently we find relatively few unfavorable dominant genes in a natural mixed population. Unfavorable recessive genes, on the other hand, may become widely spread throughout the population, since they have little or no phenotypic effect on heterozygous individuals. When we inbreed such organisms, the inbred lines soon become homozygous, as we have seen, for all their genes. In the process of inbreeding, moreover, we artificially preserve and breed individuals which might not survive under natural conditions. There is always a good chance, therefore, that the inbred line will be homozygous for several or many pairs of genes whose effects are deleterious to its vigor. These will usually, on chance, not be the same genes in different inbred lines; consequently when we cross two different inbred lines their offspring are usually more healthy and vigorous than either of the parents, since the favorable dominant genes of each line suppress the unfavorable effects of the recessive genes of the other line. It is quite possible, by selecting the most vigorous and fertile individuals of each generation for breeding, to produce a highly inbred line which is equal or superior to the average of the original mixed population in these respects. There are, moreover, as we have seen, many species of plants (and also some of the lower animals) which are almost exclusively self-fertilizing, and such organisms continue to live and reproduce in this way for countless generations with no decline in vigor. The same is true of those organisms (a number of higher plants, as well as many of the lower organisms) which reproduce by exclusively asexual methods (p. 378).

The method of selective breeding is the method by which domesticated animals and plants have been improved for human purposes. By selecting for breeding, in each generation, the individuals which have the most desirable characteristics, we gradually accumulate in one line all those genes present in the original unselected stock which affect these characteristics in the desired direction. Once the line has become homozygous for all such genes, selection can have no further effect, except as mutations may happen to occur whose effects are in the desired direction. Waiting for mutations to occur is, however, too slow a process to be of much practical utility. A more practical procedure, when no further progress is obtained by selection within one line, is to *outcross*, *i.e.*, cross the selected line to another line of different ancestry; in this way genes of both lines, favorable to the desired characteristics, may be combined and further selection may result in a new line superior to either of the original ones.

These methods of practical animal and plant breeding have been practiced empirically for centuries, without knowledge of the laws and mechanism of heredity on which their success depends. This scientific knowledge, however, recent as it is, has already proved of enormous practical value, enabling crossing and selection to be done much more intelligently, economically, and efficiently. By applying our present knowledge of the laws of segregation, assortment, linkage, etc., it is possible, in effect, to "pick apart" the hereditary characteristics of different races or varieties and recombine them in one line in any combination we may desire. The possibility of artificially increasing the frequency of mutations (p. 572) has been too recently discovered to have yet been applied for utilitarian purposes, but the future possibilities of this method are undoubtedly very great.

CHAPTER XXV

NATURAL SELECTION; THE ORIGIN OF SPECIES

Under natural conditions every species and race of organisms is constantly undergoing a process of selection. But whereas in artificial selection (described in the preceding chapter) organisms are selected for characteristics arbitrarily chosen by man for his own purposes, under natural conditions they are selected for their *ability to live and reproduce.* The mechanism and the results of this process of *natural selection* will be described in this chapter and the following one.

Multiplication of organisms.—Every kind of organism, as we have seen in previous chapters, tends to increase in numbers by reproduction. Probably the greatest rate of multiplication is found among the bacteria, some of which may, under favorable conditions, reproduce by cell division as often as once every half hour. At this rate, their numbers would be quadrupled every hour; at the end of 24 hours, the descendants of one original bacterium would number 2^{48} (about 281 million million) *if they all survived.* In many kinds of plants each individual produces millions of spores or seeds each year; among animals, in many kinds of invertebrates and of fishes each individual (or, in dioecious species, each female) produces millions of eggs per year. Among the higher animals, especially the birds and mammals, the number of eggs produced is usually much smaller, but the proportion of their offspring which survives is much larger, because of the greater care given their eggs and young (p. 406). Probably the most slowly multiplying animal is the elephant, which begins breeding when thirty years old and goes on breeding till ninety years old, producing six young in this interval, and living till one hundred years old. Even at this very slow rate of reproduction there would be, after about seven hundred and fifty years, nearly 19,000,000 elephants alive descended from a single pair, if every elephant born survived and reproduced at this rate.

Thus every kind of organism, whether its rate of multiplication be fast or slow, tends to increase *in geometrical progression:* 1, n, n^2, n^3, ... (n = rate of multiplication per generation). This is represented graphically by the first curve in Fig. 188, often called the *curve of compound interest.* It is readily seen that with this type of increase, even if the initial rate of multiplication be small, the total number of individuals rapidly becomes very large. Any species of organisms—even those with the slowest rates of reproduction—would increase until it covered the whole face of the earth, if all the offspring produced in each generation survived to maturity and reproduced in turn.

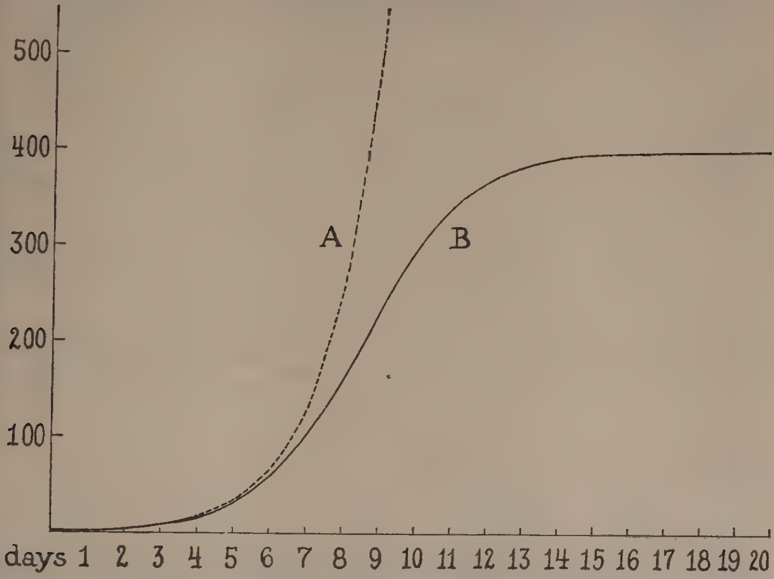


FIG. 188.—Multiplication of yeast cells: abscissae, time in days; ordinates, number of cells. *A*, theoretical rate of multiplication with unlimited space and food; *B*, actual rate of multiplication in a definite limited amount of nutrient solution.

Limitation of populations.—Needless to say, the number of individuals of any species does not actually continually increase in this way. The population (*i.e.*, total number of individuals) is limited by environmental conditions, especially by the available *food supply*. This is illustrated by the second curve in Fig. 188, representing the multiplication of yeast cells in a definite limited amount of a nutrient solution (p. 136). Under these conditions the increase follows nearly, though not quite, the compound interest curve for a short time, then the rate of increase falls off, and finally the number of cells reaches a constant value, beyond which there is no further increase. The growth of a population of any kind of organisms, under comparable conditions, gives a similar curve, as shown in Figs. 189 and 190. It is apparent from these curves that, in each case, the number of individuals reaches a constant value in a relatively short time—that is, in a few generations—and does not increase any further thereafter. It is also apparent, especially from Fig. 189, that this maximum number is determined by the environmental conditions.

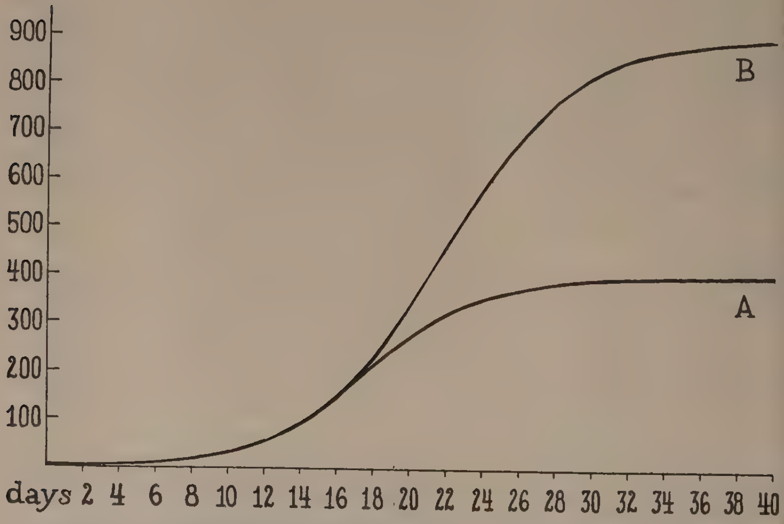


FIG. 189.—Multiplication of Drosophila: *A*, in a half-pint bottle; *B*, in a one-pint bottle. Abscissae, time in days; ordinates, number of flies.

Similarly, under natural conditions, each species of organisms rapidly increases up to the maximum number possible under the environmental conditions and then maintains this number practically constant so long as these conditions do not change. The population may fluctuate from year to year—or within shorter periods, in rapidly reproducing organisms—in accordance with fluctuations in the food supply or other environmental conditions, but, by and large, considered over a longer period, the average number remains approximately constant so long as the environmental conditions do not change permanently.

In general, the principal factor limiting the increase in numbers of any species is the limitation of its *food supply*, using this term in the broadest sense. Among green plants, the primary limiting factor is usually *light*, which is of course a prime essential in the nutrition of these organisms. In most regions, the surface of the earth is completely covered with vegetation; that is, some kind of green plant grows in every spot where it can possibly secure light. In very dry regions—*e.g.*, deserts—*water*, rather than light, may be the primary limiting factor determining the maximum number of plants. Among animals and heterotrophic plants, the

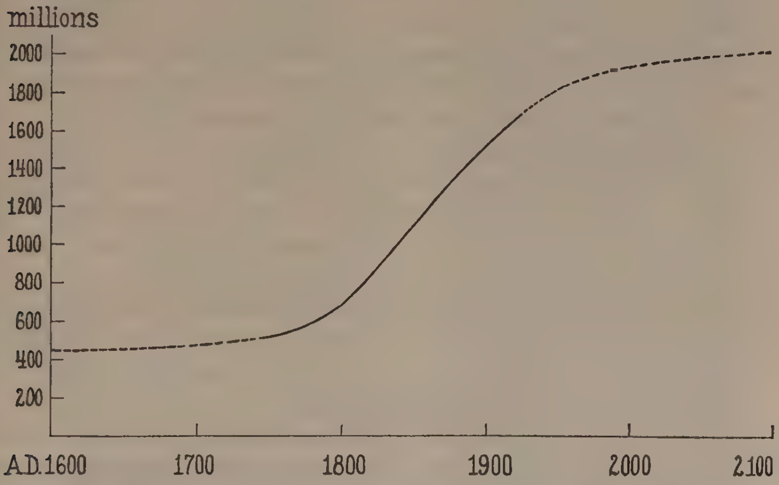


FIG. 190.—Human population of the earth: abscissae, years; ordinates, population in millions. The solid portion of the curve is based on actual data; the dotted portions are purely theoretical, calculated from the equation of the curve. The increase in population during this period, from its previous stationary level, is due to the great change in environmental conditions caused by the Industrial Revolution. The upper, dotted, portion of the curve predicts the future population on the assumption that there will be no further great environmental changes—obviously a very doubtful assumption. (Adapted from Pearl.)

primary limiting factor is usually the available amount of those organic materials which each particular species can utilize as food; though water or oxygen may be the limiting factor in some cases.

Other environmental factors which play important parts in limiting the increase of populations are *climatic* conditions, which may determine the extent of territory which a given species can occupy, and *predacious* and *parasitic* organisms which prey on it. For each particular species, under a given set of constant environmental conditions, a "balance" is attained between the tendency to increase by multiplication and the various factors limiting this increase, resulting in an approximately constant population.

The struggle for existence.—Since the processes of reproduction tend continually to increase the number of individuals, while the limitation of food supply and other environmental factors prevent this increase, only a small proportion of the individuals produced can possibly survive. Every organism is therefore constantly subject to a *struggle for existence.* This term is used in a broad and somewhat figurative sense, not as necessarily implying direct, active combat between individuals fighting for their lives. The struggle for existence, in a broad sense, includes the "struggle" of organisms against unfavorable physical conditions—cold, drought, etc.—conflict between predacious or parasitic organisms and their prey, and, above all, *competition* between organisms with similar requirements for the necessities of life. This last aspect of the struggle for existence, while often very indirect and not superficially obvious, is probably usually the most important in determining survival. It is well illustrated by a group of annual plants germinating in the spring in a limited area of ground. At first the ground is thickly covered with small seedlings; as time goes on, the number decreases while the size of the survivors increases, until finally there are but a few individuals left, completely occupying the area in which hundreds of seeds originally germinated. Each of these survivors produces a large number of seeds, and in the following spring the same struggle for existence is repeated among their offspring. Among these plants competition is primarily for "a place in the sun." Those individuals which grow a little faster overshadow the others and cut off their light, and the latter eventually die of starvation. Among animals (and heterotrophic plants) the competition is chiefly for organic food materials. It is obvious that competition must be most keen between organisms whose food requirements and other conditions of life are most similar: it must, therefore, usually be especially keen between individuals of the same species or of closely related species.

Natural selection.—What determines which individuals, of the great excess continually produced, shall survive? To a large extent, of course, it must be sheer "accident"—that is, causes having no relation to any qualities of the individual. Some seeds fall on good ground and some on stony ground—due, generally, to no virtue of the former or fault of the latter. A great many of the causes which destroy seeds and eggs, young plants and animals, wholesale—storms, predacious animals, etc.—are quite unselective in their action. Over and above this wholesale indiscriminate elimination, however, *on the average* those individuals are most likely to survive which are most *fit to live*—that is, those which are most healthy, vigorous, capable of securing food, escaping or protecting themselves from enemies, resistant to disease and unfavorable weather, etc. In other words, individual differences—*i.e.*, *variations*—play some part in determining survival; thus the struggle for existence continually exercises a *selection* among organisms in favor of those most fit to live under the conditions of their natural environment.

As we have seen in the preceding chapter, variations are, in respect to their origin, of two kinds: genetic and environmental. Selection of environmental modifications has no effect on the characteristics of the next generation, since such variations are not inherited. But selection of genetic variations tends to shift the average of the succeeding generations in the direction so selected (p. 581). To whatever extent the individual differences which determine survival under natural conditions are due to genetic variations, the effect of the "survival of the fittest" must therefore be to continually improve the average "fitness" of the race. The genetic variations of individuals can, obviously, affect the future of the race only if these individuals leave offspring; therefore, the survival of *races* is determined not only by their ability to *live* but also by their ability to *reproduce* successfully—that is, to leave, in each generation, enough *mature* offspring to at least maintain the numbers of the preceding generation. This may be effected, as we have seen in a previous chapter, either by producing a great excess of offspring or by producing a smaller number better equipped to meet the struggle for existence during their developmental stages (p. 406).

We have seen in the preceding chapter that the effects of artificial selection are usually rather limited, progress in the direction of selection ceasing when all those genes present in the original population, favorable to the desired characteristics, have been accumulated in the selected line. This limitation to artificial selection is, however, due solely to the limitation of the *time* at our disposal; we have not time to wait for "lucky" mutations in the desired direction. But natural selection knows no such limitations of time—it has "all the time there is." Generation after generation, century after century, millennium after millennium, the struggle for existence and the elimination of the less fit go on. The great majority of new genetic variations—*i.e.*, mutations—undoubtedly are unfavorable (p. 568); these are soon eliminated. Of the remainder, many, perhaps, are indifferent so far as survival value is concerned; these may survive or not—this is a matter of pure chance. But some—relatively few perhaps, and these probably almost always very slight variations (p. 568)—may confer some advantage, however slight, on their possessors, in the struggle for existence. Even of these favorable variations, many may be eliminated by "accident," but *on the average* they will increase the chances of survival, and therefore the chances of leaving descendants, of those individuals which possess them; and these individuals will, of course, transmit these mutant genes to some of their descendants, which will therefore be similarly favored in the struggle for existence. In the long run, then, every mutation which is in any way favorable to survival or reproduction stands a good chance of being permanently incorporated in the genetic constitution of the race. Comparing natural selection with artificial selection, we may say, in a general way, that artificial selection operates chiefly by the relatively rapid, but rather limited, method of selecting favorable *recombinations* of genes previously in existence; while natural selection operates chiefly by the much slower, but potentially unlimited, method of selecting favorable new mutations. This distinction is, of course, only a relative one, both of these methods being involved to some extent in both cases, since both artificial and natural selection actually select individuals with favorable phenotypic characteristics, regardless of how these are produced. The great difference between artificial and natural selection is the *time* factor: artificial selection has operated for, at most, a few centuries, natural selection for many millions of years. Natural selection is a bungling, haphazard, hit-or-miss, and therefore very slow process; but, given unlimited time, even a very slow process may produce practically unlimited results. The results of natural selection, operating throughout the past ages of life on the earth, are the organisms that exist today.

Adaptation.—The continual operation of natural selection must necessarily result in every race of organisms tending to attain and maintain the greatest possible degree of fitness to survive and reproduce. This quality of "fitness," or *adaptation*, is, indeed, one of the most striking characteristics of organisms. The manifold adaptations of organisms may be considered under two aspects: *internal* adaptation—the adjustment of the various parts and processes of the organism to each other, so that they work together harmoniously—and *external* adaptation—the adjustment of the organism to the external environmental conditions under which it naturally lives. While this distinction is by no means a sharp one, we may say, in a general way, that internal adaptation, as here defined, is the more fundamental, since it determines the ability of the organism to *live at all*, under any conditions. This aspect of adaptation is practically synonymous with *coordination*, in the broadest sense: including the coordination of developmental, nutritive, and reproductive processes as well as that of "behavior" in the usual sense, and including intracellular coordination—the regulation of metabolic processes by enzymes, etc.—as well as intercellular coordination. That this internal adaptation is usually the most important factor in determining survival is abundantly proved by our experience with mutant races, *e.g.*, in Drosophila. It has been previously noted (p. 568) that most of the larger, "visible" mutations are unfavorable; *i.e.*, these mutant forms are unable to compete successfully with the ordinary form or "wild type"—which is, of course, the reason why this particular form *is* the wild type. But, in most of these mutant forms, the visible external characteristics by which we distinguish them—such as eye-color, body-color, number or form of bristles or hairs, etc.—can have no possible effect on their ability to survive and reproduce (indeed, other species with these same external characteristics survive quite successfully); the "unfitness" of these mutant forms is due to other, internal, effects of the mutant genes (p. 518). These internal effects are, in most cases, not visible even in the internal organs; that is, they are not gross structural characteristics at all, but *functional* characteristics, dependent, presumably, on differences—perhaps very slight ones—in chemical composition or ultramicroscopic structure of some cells. These invisible, but all-important, internal effects we designate by the broad and necessarily rather vague terms "viability" and "fertility." Natural selection must—and demonstrably does—deal chiefly with such "intangible" characteristics. The failure to realize this has, probably more than any other one cause, resulted in widespread failure to understand the operation of natural selection.

External adaptations, as here defined, include all those characteristics of an organism which fit it to survive and reproduce under the particular external conditions of the environment in which it naturally lives. This includes the external mechanisms of food-getting, respiration, etc., the mechanisms of self-defense or escape, and the external mechanisms of reproduction and care of the offspring. Here, also, visible structural characteristics are no more important—probably, on the whole, less important—than the *behavior* of the organism, *i.e.*, its responses to particular environmental situations. In a previous chapter (Chapter XVII) we noted that many of the responses—tropisms, instincts, etc.—of organisms are strikingly "useful" to the organism under its natural conditions of life; we now see the explanation of this: natural selection has preserved individuals and races whose responses are useful—to themselves, of course—and eliminated those whose behavior was less favorable to their survival. The external environment of any organism is an extremely complex set of conditions, including not only the physical and chemical conditions of the non-living environment but also a multitude of other living organisms with which it comes into various kinds of relations—predatory, parasitic, cooperative (mutually beneficial), competitive, etc. So complex are these interrelations and so delicate the balance between the processes of multiplication and destruction of any particular species that the very slightest—perhaps, to us, quite inappreciable—factor may tip the scales one way or the other: determine whether the individual, the race, or the whole species shall perish or survive. It is therefore risky to say, *a priori*, that any particular characteristic of an organism is "unimportant" in respect to natural selection. It is, however, on the other hand, certainly a mistake to assume that every visible characteristic—such as color, form, and structure—must necessarily have some adaptive significance, for, as we have seen, many of these are merely incidental effects of genes which have also other, more important though less obvious, internal or invisible effects.

There has been, and is, a great deal of nonsense written on the subject of "adaptation." It is often stated, or implied, that adaptation is a primary, characteristic property of living things. This is obviously untrue. The variations of organisms are quite random, having, in general, absolutely no relation to usefulness; indeed, the great majority of them are distinctly unfavorable, and only a very small proportion are, by chance, somewhat favorable—but these few are the ones preserved and gradually accumulated by the action of natural selection. The adaptive characteristics of organisms—especially those of the type we have called external adaptations—are, in general, useful only under the particular environmental conditions under which the species has lived in the past—that is, under which it has been naturally selected—as we have previously noted in regard to behavior (Chapter XVII). A vast number of species—undoubtedly many more than now exist—have become extinct without leaving any descendants, because they failed to become sufficiently adapted; that is, they failed to have "lucky" mutations, without which natural selection can accomplish nothing but extinction. And the survivors are by no means perfectly adapted, merely sufficiently so to "get by." The adaptation of organisms is a very different sort of thing from that of machines purposefully designed to do particular things. An organism is not an economical, efficient mechanism—it is a made-over, patched-up sort of an affair, working just well enough to survive long enough, on the average, to reproduce itself. Every organism has many useless, or even positively harmful, organs and characteristics. These imperfections are the results of its method of origin: the "sorting out," by natural selection, of *chance* variations. To survive, an organism need not be perfectly adapted—merely as well adapted, on the whole, as its competitors, all of which have also been produced by the same rather crude method.

The exaggeration of the facts of adaptation has led, in recent years, to the inevitable "swing of the pendulum" to the opposite extreme: a tendency, on the part of more critical biologists, toward extreme scepticism in regard to all adaptations. While it is undoubtedly correct to refuse to regard any particular characteristic of an organism as adaptive, or "useful," until it has actually been proved to be so, there can be no doubt of the general fact of adaptation: an organism must be fit—that is, *sufficiently* fit—to survive, or it wouldn't be here. Given the unquestionable facts of (1) genetic variability and (2) the tendency of all living things to indefinite multiplication, adaptation is a *necessary*—*i.e.*, logically predictable—consequence. Every existing organism is the product of a genetic complex—*i.e.*, a group of genes—which has been "sorted out" by natural selection for millions upon millions of years. Viewed in this light, the most remarkable feature of adaptation is its imperfection. To understand this, we must clearly realize the limitations of natural selection. In the first place, natural selection can not *produce* favorable variations; it can only preserve those that occur, and their occurrence, as has been repeatedly emphasized, is a matter of chance—on the whole, a rather small chance. The possibilities of favorable variations are limited by the antecedent composition of the material: the possible ways in which any particular gene can change must be limited, and the effects of such changes on the phenotypic characters of the organism are also limited; indeed, as we have seen, any very great effect of a single mutation is most likely to be fatal. Natural selection is thus largely restricted to relatively small changes, and must therefore work very slowly. The particulate nature of heredity is also a decided limitation on the perfection of adaptations: each gene, as we have seen, produces several or many phenotypic effects; some of these may be favorable, others indifferent or unfavorable, but they must be "taken or left" all together—an organism inherits, not phenotypic characters, but genes. This undoubtedly explains the great number of useless—or even harmful—characteristics of organisms. Moreover, natural selection can not even select organisms for particular genes, as artificial selection can; it must select them for their ability to survive *as a whole.* The survival of any particular individual or race is determined, not by the perfection of any one characteristic, but by the aggregate fitness of all its characteristics. As we have emphasized above, the general qualities of viability and fertility will usually be more important in determining survival than any precise adaptation of particular parts or functions. Hence arises the apparently unfavorable comparison of an organism with a purposefully designed machine: the organism can not do any one thing as *efficiently*—but it can do more different things, and, above all, it can perpetuate its kind. The same kind of comparison may be made between natural races of organisms and cultivated races produced by artificial selection: the latter are always superior in some one characteristic for which they have been especially selected—they can produce milk, or eggs, or fruit, more efficiently—but they can seldom survive in free competition with the natural races. The explanation of this difference, of course, is that the natural races have not been selected for their ability to do any one special thing efficiently, but for their ability to *survive.* This is the only quality for which natural selection *can* select organisms. To this end, it is effective—because it has practically unlimited time and materials (*i.e.*, individuals) at its disposal—but it is by no means an economical or intelligent process, and its results are far from perfect.

The origin of species.—Since the great majority of new variations—*i.e.*, mutations—are probably unfavorable (at least in the more complex organisms), the chief effect of natural selection must be to preserve *uniformity* of each species, by eliminating most of these new variations. That this is, in general, true is confirmed by comparing wild with domesticated species: the latter usually seem to be more variable; this is because the action of natural selection is largely prevented, and relatively inviable variants are artificially preserved. This difference, however, relates largely to the more conspicuous variations, often due to relatively large effects of single mutations, which, as we have seen, are especially apt to be inviable. Every wild species is found to be genetically heterogeneous for many genes with relatively slight effects, so that natural selection apparently "tolerates" many *slight* mutations.

Any species which has inhabited a particular environment for a great many generations may be supposed to have become, by the action of natural selection, about as well adapted as the inherent limitations of the material—that is, its possibilities of viable mutations—permit. We should expect, therefore, under these conditions, to find species persisting for long periods of time without any appreciable change in their *average* characteristics; and this is, indeed, what we do find in many cases. This is true, however, only so long as the *environment* does not change. Considered over periods of a few years or even a few centuries, most "natural" environments (*i.e.*, those not modified by the activities of man) seem to remain quite constant or, at least, to merely fluctuate with the seasons, etc., about a constant average condition. Considered over longer periods, however, practically every environment undergoes great changes. The most obvious of these are geological and climatic changes. Even within the period of human history—an extremely short time in the history of the earth—certain regions (*e.g.*, in Asia) which once supported flourishing civilizations have become deserts, due to climatic changes. Going back some few thousand years further—still within the existence of the human species—vast regions of the earth (*e.g.*, in North America, Europe, and Asia) were several times subject to completely arctic conditions, alternating with periods of tropical or subtropical conditions. And if we look further back into geological time—millions of years—we see continents rising and sinking, changing their outlines and connections, mountain ranges elevated and worn down, etc., so that we may say that practically every spot on the surface of the earth has, at some time during the period within which life has existed, presented every possible environmental condition—salt water, fresh water, high land, low land, cold, hot, and temperate. But these great physical changes, while the most impressive, are by no means the only important environmental changes. We have noted that the effective environment of any organism consists no less of *other organisms* than of non-living factors. Indeed, because of the complexity of their interrelations and the fact that *competition* is usually the most decisive aspect of the struggle for existence, the relations of organism to organism are, in general, the most important of all environmental relations. Whenever one species invades a new territory, increases or decreases in numbers, or changes its mode of life in any respect, a multitude of other organisms are likely to be affected directly or indirectly. The most obvious examples of this are the migrations of man, with the numerous dependents and "camp-followers" which accompany or follow him. Many other essentially similar, though usually less extensive, changes undoubtedly occur in nature, due to "accidental" transportation of organisms from one region to another, extension of the range of a species by slight, perhaps temporary, climatic changes, decrease or extinction of a species by disease, increase in numbers due to one of the rare "lucky" mutations, etc.

Whenever any change of the effective environment occurs, due to any of the causes mentioned or others, it may affect various species in different ways: some species, unfavorably affected, may decline in numbers or even become extinct; other species, favorably affected, may increase in numbers and extend their range; in some species, slight variations already in existence but hitherto barely "tolerated" by natural selection may gain some advantage by the changed conditions and thus increase in numbers, perhaps eventually replacing the parent form; etc. When a species increases in numbers, since a greater proportion of its offspring survives a greater number of its variations will be "tolerated," and some of these may, by chance, be better adapted to a slightly different environment, thus extending the geographical or the ecological range of the species. When, on the other hand, a species strikes "hard times" and its numbers decrease, some of its varieties may be more adversely affected than others and may be wiped out, leaving the few remaining ones as sharply distinct varieties or incipient species. As environmental conditions, such as weather, are always fluctuating back and forth, these two processes must occur alternately with all species to a greater or less extent: increase of numbers, range, and varieties in "good times," decrease of numbers and splitting up of the species in "hard times." Climatic or other environmental changes may often wipe out a species entirely in some parts of its range, leaving it in separate isolated groups in other parts; this factor of *geographical isolation* plays a very large part in species formation, as we shall note again later. All these various kinds of changes in species, so closely dependent on environmental changes, give the impression, especially when the results are viewed over great periods of time, that the environment is actually the *cause* of these changes—and so, in a sense, it is, but it is the *selective* action of the environment, not its direct *modifying* effect on individuals (p. 539), which modifies the characteristics of the species. The direct effects of the environment on individual development *are not inherited* (p. 574), and therefore cannot permanently affect the characteristics of the species. Environmental changes, in general, can not cause *genetic* variations; in some cases—*e.g.*, temperature changes—they may affect the frequency of occurrence of such variations, but these variations will certainly not have any special adaptive relation to such environmental factors. The essential rôle of the environment in the formation of new species is to determine which varieties, or incipient species, shall survive—and to make room for them by extinguishing other species.

The effects of natural selection, acting over long periods of time, under the various conditions discussed above, on a group of related organisms are represented diagrammatically in Fig. 191. The intervals between the successive vertical lines may each represent, let us say, a thousand generations. The letters at the left may represent a group of closely related species or—going one step further back—isolated varieties of a single species. Each of these species is continually producing new varieties, by mutations; most of these are quickly eliminated by natural selection; some of them persist for longer periods of varying length. In the course of the ten thousand generations represented in our diagram, the several original species may meet different fates, as indicated in the figure. One species has given rise to several new forms, while the original form has disappeared; in another case, the original form has persisted practically unchanged while all its offshoots have perished; in a third species, both the parent form and some of its offshoots have persisted; the other species of the original group have become entirely extinct, after shorter or longer periods, leaving no descendants. Thus, after ten thousand generations we may have no greater number of distinct forms—species or varieties—than at the beginning, though a much greater number have appeared and disappeared in the meantime; but the surviving forms are related to each other in varying degrees, due to their method of origin, as indicated in the diagram, and they differ from each other, on the whole, more than did the original forms, as indicated by their greater distance apart in the diagram. Thus our original group of varieties or closely related species has become a number of sharply distinct, more distantly related, species, tending to form several larger groups; after another ten thousand or hundred thousand generations, perhaps, these groups will have become distinct genera, each containing several species; and so on. Thus, through the ages, the action of natural selection under varying environmental conditions continues, by diversification and extinction, to make new species, split them up, modify them, wipe them out—resulting in the great number of variously adapted and variously related species which inhabit the earth today, and the vastly greater number which have come and gone.

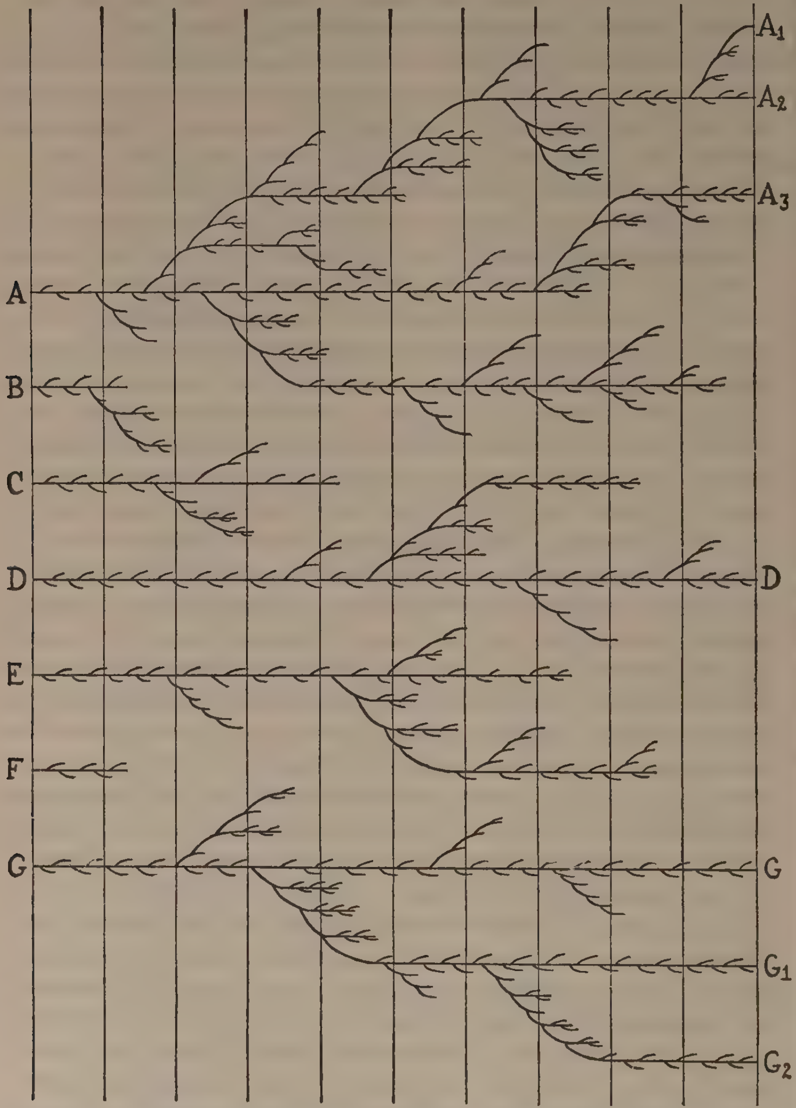


FIG. 191.—Diagram illustrating the origin and extinction of varieties and species by natural selection. The horizontal dimension represents time (*i.e.*, the succession of generations), the vertical dimension variation. The very short branches represent the numerous mutations which are quickly eliminated by natural selection, the longer branches those which persist for longer periods. (Adapted from Darwin.)

That species (and larger groups) do actually originate in this way—by the slow accumulation of numerous slight mutational differences—is clearly indicated by a comparison of the distinctive characteristics of species with those of mutant races of any one species. In the species Drosophila melanogaster we have several hundred sharply distinguishable races each differing from the "wild type" by one or a few genes *known* to have originated by mutation. The visible differences between these races are of the same *kinds* as the differences between the various species of the genus Drosophila and of other genera and families of flies. Among the most frequent types of mutational and also of specific differences are: differences in size, color, and pattern of the body; size, shape, texture, and color of the eyes; number, size, and distribution of bristles and hairs; size, shape, color, and venation of the wings. Various other types of external effects of mutations, though less frequent, are also of the same kinds as the differences used to distinguish species, genera, and families. The changes effected by mutations, as we have seen (p. 567), may be of any degree, from types that differ so slightly that statistical methods are necessary for the detection of any differences at all, to such extreme forms as eyeless or wingless races. There is, however, one characteristic difference between the diversity shown by the various mutant races of a single species and the diversity shown by a group of wild species: the mutant races often differ strikingly in a few characters and are alike in all others, while the species usually differ slightly in many characters but are not strikingly different in any one. This is obviously what we should expect from what we have previously learned about mutations: in general, the greater the effect of a single mutation, the more likely it is to be relatively, or even completely, inviable (p. 568). Mutations which bring about relatively slight changes are least likely to be harmful and therefore most likely to be preserved by natural selection. Hence it results that the differences between wild species consist, usually, of many slight mutational differences, slowly accumulated over a long time, rather than a few larger ones. Such slight mutations also occur in our experimental cultures, probably more frequently than the larger ones, but the latter are artificially selected and preserved because they are more convenient to work with in the study of heredity. It should be clearly realized, of course, as we have repeatedly emphasized, that the slight external differences by which we classify organisms into species, genera, etc., are probably, for the most part, of no direct significance in natural selection, but are merely incidental effects of genes which also affect other, more important, characteristics by which the different species are adapted to slightly different environments or methods of getting a living.

Not only the kinds of differences which distinguish *species*, *genera*, or *families*, but also such differences as characterize larger groups, such as *orders* or *classes*, are known to arise by mutation. For instance, in Drosophila, mutations have several times produced races with *four wings;* the possession of only two wings is a distinctive characteristic of the whole order (Diptera) to which this species belongs, distinguishing it from other orders of insects which have four wings. Again, mutations have produced races of Drosophila with *more than six legs;* the possession of only six legs is a distinctive characteristic of the whole class (Insecta) to which this species belongs, distinguishing it from other classes of arthropods which have more than six legs. It is not for a moment suggested that new classes or orders have arisen in this way, by single mutations, because such large sudden changes are almost invariably relatively inviable and could not survive under natural conditions; these cases are mentioned merely to show that the *kinds* of differences which distinguish these large groups of organisms do arise by mutation. It is not *impossible*, of course, that such large mutations may have occasionally survived; it is conceivable, for instance, that the advantage of a large change which enabled the mutant form to inhabit a different kind of environment, thus escaping the pressure of competition, might outweigh the disadvantage of decreased general viability; such events are, however, extremely unlikely, and must be, at best, very rare. Generally speaking, the formation of new species, genera, families, etc., undoubtedly occurs very gradually by the slow accumulation, over vast periods of time, of numerous very small differences originating by *slight* mutations.

Whenever distinct species can be crossed successfully, they are usually found to differ from each other in many genes, these differences being inherited in exactly the same ways as genetic differences within a species which are, in many cases, definitely known to have originated by mutations (or by chromosome aberrations). In a few cases, forms classified as distinct species differ from each other by only one genetic difference, of the type produced by a single relatively large mutation, but as a rule such forms are not recognized as distinct species.

Interspecific sterility and isolation.—It will be apparent from the foregoing that no sharp distinction can be made between *races* or *varieties*, on the one hand, and *species* on the other hand. These terms—as also the terms *genus*, *family*, etc.—are essentially arbitrary categories into which organisms are classified for convenience, indicating various degrees of resemblance corresponding, in a general way, to degrees of genetic relationship among them (p. 36). There is no possible general definition of a species except a group of organisms which the experts on the subject agree to call a species—and the experts very frequently, alas, do not agree. In general, however, we may say that the differences between species are more constant—that is, there are fewer intermediate forms—than between varieties of the same species. This is due to the fact that, as a rule, different varieties of the same species interbreed freely, and the descendants of such crosses include, of course, every possible recombination of the various genes in which the varieties differ; while different species, generally speaking, either can not or do not interbreed freely, so that there are relatively few or no intermediate forms. *Interspecific sterility*, to a greater or less degree, is a fairly general rule. By interspecific sterility is meant either that two species when crossed do not produce viable offspring, or that these offspring (*species hybrids*) are themselves sterile. Both of these conditions occur in every intermediate degree, in different species crosses, from complete fertility, equal to that of either pure species, to complete sterility. Various degrees of sterility are also sometimes, though not generally, found between races of the same species—sometimes between races which have absolutely no visible differences.

Such mutually sterile races are undoubtedly to be regarded as incipient species.

Interspecific or interracial sterility is due to various causes in different cases. In some cases, as we have previously seen (p. 419), the sperm of one species may activate the egg of another, but the chromosomes of the sperm never grow or divide at all in this egg, or they may do so for a short time and then be eliminated partially or entirely; the genes of the paternal species are evidently unable to grow and reproduce themselves normally in the foreign cytoplasm (p. 543). In other interspecific crosses, the visible behavior of the chromosomes is normal, but the embryo does not develop normally and perishes before reaching maturity; the two sets of genes evidently produce conflicting effects; such cases are comparable to failure of development due to abnormal temperatures or other environmental factors (p. 540). In some cases the hybrid develops normally in most respects, but the germ cells and the gonads fail to develop normally, so that the hybrid is sterile; such cases are not essentially different from those in which the hybrid is inviable—it merely happens that, in these cases, the particular organs which are most adversely affected are not essential to the life of the *individual.* In other cases of viable hybrids, the germ cells develop normally up to the time of synapsis, but the paternal and maternal chromosomes do not synapse normally, are distributed irregularly at the reduction division, and the gametes—or many of them, at least—are consequently inviable or infertile. Such cases are most frequent when the chromosomes of the two species, or races, differ in number—we have noted such cases previously, *e.g.*, in crosses of diploid and tetraploid forms (p. 560)—but they also occur in some cases where there are no *visible* differences between the two sets of chromosomes; in such cases the behavior of the chromosomes at synapsis indicates that they contain different sets of genes—*i.e.*, what *appear* to be homologous chromosomes are really not. All these various causes of interspecific or interracial sterility might be included under the general term "incompatibility of genetic constitutions," which may mean either differences between the genes of the two forms or different distributions of the genes among their chromosomes.

How does interspecific sterility originate? One obvious method is by certain types of chromosome aberrations (p. 559). We have seen, for instance, that diploid and tetraploid races, each fertile by themselves, give triploid offspring when crossed, which are largely sterile (p. 560). Some other types of chromosome aberrations—*e.g.*, translocations—might also give races each of which would be perfectly fertile by itself but whose hybrids would be largely sterile. Different species, often closely related species, do have differences in number, size, and shape of their chromosomes, and in the locations of corresponding genes in their chromosomes, showing that chromosome aberrations of various kinds must have occurred and been perpetuated at some time during their history; but not all of these aberrations need necessarily have any direct relation to interspecific sterility.

Mutual sterility may, however, also exist between species, or races, which have no visible differences in their chromosomes. In the cases in which the genetic basis of this sterility has been studied, it is found to be due to differences in several or many genes. In no case (with one possible exception) has any considerable degree of interracial sterility been known to originate by a single gene mutation. In general, interspecific sterility or "incompatibility of genetic constitutions" seems to be a consequence of differences in many genes. The degree of interspecific sterility is not necessarily proportional to the visible differences between the species, but, in general, it increases with the remoteness of their relationship; *e.g.*, it is more general and, on the average, more complete between species of different genera than between those of the same genus, and between species of different families there is almost always complete mutual sterility. This merely means that the more differences there are between the genes of two species, the more likely are these differences to produce some incompatibility in fertilization, development of the hybrid, or of its germ cells.

The question then is: how do the genetic differences between two groups of organisms, descended from a common ancestor, accumulate up to the point of mutual sterility? Unless a considerable degree of interracial sterility originates suddenly (as may occasionally happen by chromosome aberrations, as explained above), the two races must be effectively *isolated* from each other in some other way during this period; for if they interbred freely, producing perfectly fertile offspring, the continual recombinations of genes must tend to distribute all the genes throughout the whole population, and no distinct races differing from each other in many genes could develop. The most obvious—and probably, on the whole, the most important—means of isolation is *geographical isolation.* Any extensive area in which a species can not live constitutes an effective geographical barrier between populations of that species; *e.g.*, large bodies of water are effective barriers to most terrestrial organisms, large bodies of land to aquatic organisms, cold regions to organisms which can live only in warm climates, hot regions to those which live only in cool climates, etc. That geographical isolation is actually a very potent factor in species formation is conclusively shown by the geographical distribution of organisms: we frequently find a single species distributed throughout a very extensive continuous area—*e.g.*, the greater part of a continent or ocean—while the same group is represented by several distinct though closely related species within much smaller but discontinuous areas—*e.g.*, a group of islands, isolated valleys, or inland waters. On the other hand we often find distinct but closely related species occupying the same territory; these may, however, in many cases, have been isolated from each other during the period when they were gradually becoming distinct species, for, as we have previously noted (p. 602), the environmental factors which determine the geographical distribution of organisms often change greatly in the course of time. Most organisms never wander very far from the place where they are born; even birds which migrate thousands of miles return to the same spot every year to mate and breed; therefore even relatively small areas uninhabited by a species may act as fairly effective barriers between populations of that species. Races which inhabit slightly different environments within the same general territory may also be effectively isolated from each other. For all these reasons, geographical isolation probably plays an even greater part in species formation than it appears, superficially, to do.

Another means of isolation is what may be called *temporal isolation:* differences in the reproductive seasons of different races. There are many examples of such differences between closely related species and between varieties of the same species. Such races are effectively isolated from each other, even though growing side by side, because they can not interbreed.

Another means of isolation is what has been called "*psychological*" *isolation:* the refusal of two races to interbreed. This is a striking feature of the behavior of many animals—even relatively "low" ones, such as insects—the individuals of one species, more especially the females, refusing to mate with individuals of another, closely related —often, to us, almost indistinguishable—species. How great a part this may play in the initial separation of species, by the reproductive isolation of groups within a species, is doubtful.

In *self-fertilizing* species, each individual is practically isolated reproductively. This is clearly shown by the fact that such species are usually found, under natural conditions, to consist of a number of pure lines (p. 583), which may grow close together yet remain genetically distinct. That this condition favors the splitting up of species is indicated by the fact that we often find, in groups of organisms which are chiefly self-fertilizing, a large number of distinct but only slightly different species. A somewhat similar condition obtains in dioecious organisms which, because of their breeding habits, are rather closely *inbred* (p. 587). This is true, for instance, in most ants, because the sexual individuals usually mate with others from the same nest, *i.e.*, their own brothers or sisters; in this group we find many slightly different forms, commonly called varieties or subspecies but really quite as distinct as many forms which, in other groups, are called species.

Whenever two groups of individuals are effectively isolated from each other reproductively, they must, on the average, tend to become genetically different, by the accumulation of different mutations. For, no matter how many of the mutations which occur and are preserved are identical in the two groups, *some* must, by chance, be different, and therefore the genetic differences between the two groups will, on the whole, tend to increase the longer they are isolated. If the two groups are subject to different environmental conditions in any respect, their divergence may be hastened by natural selection. Moreover, if the two groups come into competitive relations with each other in any way (which will usually be the case whenever their separation is due to other than strictly geographical factors), the action of natural selection must, on the whole, tend to favor their divergence; for the more they differ the less direct, on the average, will be their competition with each other, and therefore the better chance, other things being equal, will each have to survive. The more the two groups come to differ genetically the more apt are they to have some incompatibility of genetic constitutions, resulting in inviability or infertility of their hybrids. Once any large degree of mutual sterility has developed (whether gradually or suddenly), this is itself, of course, a most effective means of genetic isolation; and the two races will continue, with the passage of time, to accumulate further genetic differences. When interspecific sterility has become complete, or virtually so, the two species are henceforth completely isolated genetically, regardless of what opportunities they may have to interbreed, and each will pursue its future development independently, just as any other distinct species. Their subsequent divergence into different genera, families, orders, etc., is then merely a matter of time, chance, and the action of natural selection under varying environmental conditions.

Natural selection and modern genetics.—The origin of species by means of natural selection was first explained by Darwin in 1859. At that time nothing was known of the laws or mechanisms of heredity and variation. Darwin based his explanation on the unquestionable facts that all organisms do vary, that *some* variations are inherited, and that large variations are, in general, less viable than slighter ones. Since then—chiefly in the last twenty years—the mechanism of heredity has been completely elucidated and a good deal has been learned as to the nature and origin of variations. The effects of this modern knowledge on the theory of natural selection have been: (1) to clarify our ideas as to what *kinds* of variations furnish the material for natural selection to work on; (2) to completely remove the chief objections to the theory of natural selection; (3) to disprove the other theories which have been proposed to account for the origin of species.

(1) The modern study of heredity and variation has led to clear distinctions among the several causes of variation (p. 557). The most fundamental of these distinctions is that between genetic variations and environmental modifications. These two types of variations, while often similar in their visible effects on the individual, differ essentially in their origin and in the all-important respect of *heritability*. Since environmental modifications are not inherited they can, of course, play no part in altering *racial* characteristics or in the origin of species. The greatest part of the *genetic* variability which we ordinarily observe within a species is due to *recombinations* of genes by the normal operation of the mechanism of heredity in sexually reproducing organisms. These recombinations, as we have seen (p. 588), play a very large part in artificial selection, and undoubtedly in natural selection also, since certain combinations of genes produce more favorable phenotypic characteristics than others. Such recombinations, however, obviously can not account in any large degree for the origin of species, since they produce nothing essentially *new;* the recombinations resulting from crosses of different races of one species could hardly produce a new species. Interspecific hybridization may sometimes produce new species: in some cases the crossing of two species (especially when these differ in the number or make-up of their chromosomes) may produce hybrids of a stable type which thereafter remains distinct from both of the parent species; and some forms recognized as distinct species have undoubtedly originated in this way. It is obvious, however, that this can not be a major factor in the origin of species, since distinct species must already exist before interspecific hybridization can occur, and the hybrid species so produced must, in general, be more or less intermediate between the parent species in their character-

istics. The same considerations apply, to a large extent, to *chromosome aberrations*, which are merely abnormal—*i.e.*, unusual—recombinations of previously existing genes. Certain of these aberrations—those which give viable and genetically stable types—may, as we have previously seen (p. 611), play a part in the origin of interspecific sterility, but they do not of themselves, as a rule, give rise to phenotypic differences of the kinds that distinguish species. The origin of the differences between different kinds of organisms must be ascribed chiefly to *changes of the genes* themselves—*i.e.*, mutations. The evidence that the differences between species are actually of this nature has been presented previously (p. 607). Our knowledge of the nature and cause of mutations is still very incomplete (p. 573); but we know that they are *random* changes, in the sense that they may affect any characteristic of the organism in any direction and to any extent, that they have no relation to "usefulness" and are not correlated with any particular environmental conditions. The usefulness of any particular mutational change and its relation to environmental conditions determine its *survival*, but not its origin. We have noted several times in the preceding pages that relatively large mutational changes, while they play an important part in artificial selection, can not, as a rule, be of much importance in natural selection, because they are usually relatively inviable; the origin of species must be effected chiefly by the slow accumulation of relatively slight mutational changes which *happen* to be advantageous to the organism. Summarizing: the variations which furnish the materials for natural selection to work on are *heritable*, *random*, and chiefly *slight* variations—which is exactly what Darwin said. What modern genetics has added to this is some knowledge of the nature of such variations: they are due primarily to changes in individual genes, which we call mutations.

(2) The chief objections to the theory of natural selection, before the mechanism of heredity was understood, were: that this theory could not account for the many useless characteristics of organisms, such as most of the *visible* differences between species are; and that slight variations would be lost by "dilution" when the variant individuals

crossed with the more numerous individuals of the original type. Both of these objections are completely eliminated by our present knowledge of heredity. As we have noted previously, the visible differences between species are, to a large extent, of no significance in natural selection, but are incidental effects of the *same genes* which produce other, usually invisible, effects of great importance for survival. The idea of "dilution" of variations was based on the assumption that the hereditary material is indefinitely divisible and heredity is a process of "mixing"; we now know that this assumption is absolutely incorrect. When mutant individuals cross with the original type, the result is the distribution of the mutant gene through the population without in any way altering this gene itself. If the mutant gene is recessive, the action of natural selection will be, at first, somewhat slower than if it were dominant: if it is unfavorable, it will not be eliminated as quickly, and if it is favorable it will not replace the original allelomorph as quickly, because natural selection can only act on individuals homozygous for the recessive gene. For this reason, we often find unfavorable recessive genes, but seldom unfavorable dominant genes, in natural populations (p. 587).

(3) Other theories which have been proposed to account for the origin of species are no longer of any significance, as they have been proved incorrect by our modern knowledge of heredity and variation. One of these was the idea of a cumulative *direct* effect of the environment in modifying species; this was based on the assumption that "acquired characters"—*i.e.*, environmental modifications—can be inherited, which has now been completely disproved (p. 574). Another was the idea of "orthogenesis": that a race of organisms might have an "innate tendency" to keep on varying further and further in a particular direction. All our experience with variation negatives this idea; all genetic variation is quite random—any race is as likely to vary in any direction as in any other. The race as a whole may continue to change progressively in a particular direction; but this is due solely to the action of natural selection preserving variations in this direction and eliminating all others.

The effect of modern genetics on the theory of natural selection has thus been to somewhat clarify and to greatly strengthen it, without essentially modifying this theory as developed by Darwin. Natural selection seems entirely adequate, in conjunction with the known facts of variation and heredity, to account for the origin of species; and, so far as we can see, there is no other way in which the present species of organisms can have originated.

CHAPTER XXVI

RESULTS OF EVOLUTION

THE origin of species by descent, with variation, from other, previously existing, species is called *organic evolution.* This term is generally understood to imply the origin of all existing organisms by descent from one or a few original species of very simple organisms, though it does not necessarily imply this. Every mutation, every change in the average characteristics of a race by selection, artificial or natural, is a process of evolution. In this sense evolution is directly demonstrable by experiment, as we have seen in the preceding chapters. That all the species of organisms now existing have originated by similar processes in the past is an inference which can not, in the nature of the case, be directly proved by experiment. This inference, however, is justified by the fundamental scientific principle of the *uniformity of nature:* under similar conditions, similar causes produce similar effects. Evidence from geology and physics (p. 638) indicates that organisms have lived on the earth for at least 1,000,000,000 years—probably much longer—and that the conditions of life have been similar, in a broad sense, throughout this time, to those of the present. If we multiply, so to speak, the processes of evolution —*i.e.*, variation and selection—demonstrably going on at present, by the length of time during which life has existed and during which these same processes have presumably been going on, the logically predictable result is a great variety of very diverse kinds of organisms, such as actually exists today. We can, however, go much further than this in correlating the necessary results of evolution with observed facts. For the origin of diverse kinds of organisms by variation and selection must result in certain general relations in respect to the resemblances and differences among existing species and between the present species and those of past ages, in respect to the geographical distribution of the various kinds of organisms, etc. There are, in fact, a great number of observed relations of this kind, readily interpreted as results of evolution, and apparently inconsistent with any other interpretation. The theory of organic evolution, in its broader implications, has therefore essentially the same kind of justification as any other scientific theory—its ability to correlate and explain numerous observed facts which would otherwise be unrelated and meaningless. A few of these classes of facts, which seem to be necessary results of evolution, will be mentioned briefly in this chapter.

Resemblances and differences among organisms: classification.—It is a familiar fact that various degrees of resemblance and difference exist among the many kinds of living organisms. As we have previously noted, organisms are *classified*, in accordance with these different degrees of similarity, into groups and sub-groups: kingdoms, phyla, classes, etc. (p. 36). Of course, any collection of objects, which are not all identical, can be classified according to arbitrarily selected characteristics. The classification of organisms is, however, quite a different sort of thing from such a purely arbitrary, or "artificial," classification. For we find that all the organisms of any one group—of whatever magnitude—resemble each other, and differ from those of other groups, not merely in one characteristic but in many. Organisms which have been originally classified together on the basis of certain characteristics—such as gross structures—are usually found, on further study, to resemble each other also in other characteristics—chemical, developmental, etc.—which may have been entirely unknown to those who first classified these organisms. Such facts indicate some real, natural relations underlying the system of classification. The avowed intent, in fact, of the "natural" classification of organisms is to coincide, as nearly as possible, with the presumed genetic relations of the organisms, *i.e.*, to group together those organisms most nearly related by descent. Thus we always classify the two sexes together, however much they may differ in appearance, because we know them to be offspring of the same parents. Similarly we classify together different generations—*e.g.*, gametophyte and sporophyte—which may differ in almost every visible characteristic, because we know that each produces the other. Also, we classify as one species varieties or breeds—such as those of many domestic animals and plants—which may differ strikingly in some characteristics, because they all interbreed freely, which is presumably a good indication of fairly close relationship. With organisms of different species—except, in some cases, rather closely related species—our only practical criteria of relationship are their phenotypic resemblances, because, in general, such organisms can not be interbred (p. 609). On the average, those organisms most closely related by descent will have the most genes in common; also, on the average, those organisms having most genes in common will have the most phenotypic resemblances. Of course, there are exceptions to both these rules: identical genes may arise independently, by mutations, in quite unrelated (or very distantly related) races; also, identical (or indistinguishable) phenotypic characteristics may be produced by entirely different genes or combinations of genes. For these reasons, resemblance in one or a few characteristics is not necessarily a criterion of genetic relationship. But it is improbable, on chance, that such coincidences should occur frequently in any particular case; therefore the more characteristics two organisms, or groups of organisms, have in common, the more probable it is that their resemblances are due to similarities of genetic constitution, and that these genotypic similarities are due to relationship by descent from a common ancestor from which they have derived these common genes. Wherever we can test the question experimentally, by breeding tests, —which is, of course, the only conclusive method of proving genetic relationship—those organisms which have been classified together most closely, on the basis of their presumed relationship as judged by phenotypic resemblances, are, in general, found to be actually most closely related genetically, *i.e.*, to have most genes in common (p. 607). Since the system of classification antedates modern genetic methods, these facts strongly indicate that its criteria of relationship are, on the whole, fairly sound ones.

If all existing kinds of organisms have been produced by the gradual accumulation, by natural selection, of slight mutations, it is evident that classification—that is, the division of organisms into fairly well-defined groups—is only possible at all because many intermediate types have become extinct. If every type (*i.e.*, every species, variety, and individual variation) of organism that has ever lived were alive today, there would be no definable groups at all, but a continuous series of intermediate forms connecting every type of organism with every other type. Since our classification thus depends on the accidents, so to speak, of extinction, we should expect to find it not a neat, symmetrical scheme, but rather a confusing jumble of large and small, well- and ill-defined, groups—as, in fact, we do. The living races of organisms have often, and quite aptly, been compared to the surviving twigs of a tree of which the main limbs and branches are dead and, for the most part, lost to our view. The task of a "natural" classification is to attempt to assign each twig to its proper limb and branch—that is, those from which it originated—on the basis of the resemblances and differences among the living forms, aided, in some cases, by a relatively few, more or less imperfect, remains of extinct forms (p. 636). Under these circumstances, it is scarcely surprising that there are many uncertainties and differences of opinion. In some cases major groups are connected by a series of intermediate forms, so that it is difficult—or, in fact, impossible, except arbitrarily—to draw the line between them. We have seen one striking example of this in the case of the two primary divisions (kingdoms) of organisms, plants and animals, which are perfectly connected by intermediate forms such as the flagellates. In other cases, the opposite difficulty arises: there has been so much extinction that certain small groups of organisms are left very isolated, with no obvious relations to any of the larger groups. There are a number of classes of worm-like animals in this position. In such cases, of course, our classification must be somewhat arbitrary, and will be decided, in practice, largely by considerations of convenience, such as the desirability of keeping the number of main groups (*i.e.*, kingdoms and phyla) as small as possible. The question naturally arises: why—since the primary object of classification is convenience—do we not, for practical purposes, abandon the attempt at a "natural" classification and adopt a purely arbitrary, but simpler, scheme? The answer is that it has been found by experience that the "natural" classification is, on the whole, the most convenient one—for the very reason that it groups together those organisms which have the *most* characteristics in common.

We shall now mention briefly some of the kinds of phenotypic characteristics on which classification is based, and which are presumed to afford criteria of genetic relationships.

Structural characters: homologous organs.—Classification has been largely based on visible structures, especially, in the larger organisms, macroscopic structures, since these are the most easily studied characteristics. We can readily recognize, throughout large groups of organisms, organs with fundamental similarities of structure, despite numerous differences in details (Fig. 192). Such organs are said to be *homologous.* By this is meant that they show numerous similarities in the nature and arrangement of their parts, in their structural relations to other organs, and in their mode of development, *not necessarily correlated with similarities in function.* The differences between the homologous organs of different species are usually directly correlated with differences in their functions—and thus explainable by natural selection—while their similarities seem to have no rational explanation other than genetic relationship. This idea is often expressed by saying that the fundamental similarities of these organs are due to the fact that they have been "derived," with more or less modification, from the same organ of a common ancestor. A moment's reflection, however, is sufficient to show that this statement is a purely figurative one, for all the organs of each individual are, of course, actually derived from a single cell (*e.g.*, a zygote or a spore), which has, in turn, been derived solely from the germ-cells—not from any somatic organs—of its ancestors. The real reason for these similarities, if they are due to genetic relationship, must be that many of the genes responsible for the structural characteristics of these organs are identical in these various organisms. This, as we have seen, can not, in general, be directly proved (except for very closely related species), but can only be inferred

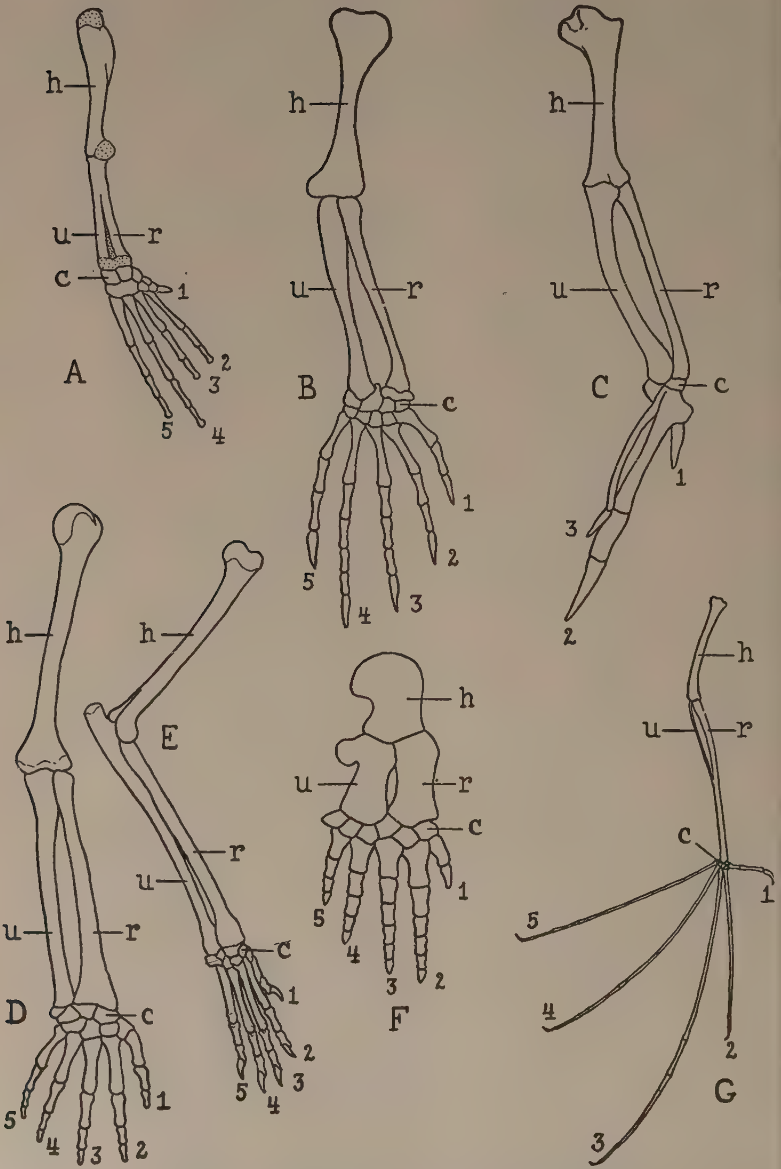

h
u
r
c
1
2
3
4
5
A
B
C
D
E
F
G

FIG. 192.—Skeletons of fore-limbs of various vertebrates: *A*, frog; *B*, lizard; *C*, bird; *D*, man; *E*, cat; *F*, whale; *G*, bat. *h*, humerus; *r*, radius; *u*, ulna; *c*, carpus; *1–5*, digits.

from the structural similarities themselves. There is, obviously, some danger here of "arguing in a circle": the organs are homologous because the organisms are related, and the organisms are related because the organs are homologous. It must be remembered, however, that in general our classification and presumptions of genetic relationship are based on similarities not in one organ only but in many. Thus, while we might easily be led to very erroneous conclusions if we based our ideas of genetic relationship on similarities in one organ—since such similarities might be purely "accidental," as explained above (p. 621)—there is much less danger of this when our conclusions are based on similarities in many organs, since it is highly improbable that so many similar structures can have arisen independently in unrelated races.

It has been mentioned above that the differences between the homologous organs of different species are usually directly correlated with differences in the functions of these organs—due to differences in habitat or mode of life of the organisms—while their similarities seem to be due to persistence of common genes derived from a remote common ancestor. On the other hand, we may find similarities of structure in organs having similar functions in quite unrelated (or very distantly related) organisms; such organs are said to be *analogous*. Thus the differences between the fore-limbs of various vertebrates (Fig. 192) are obviously correlated with their different functions—walking, swimming, flying, etc.—while their underlying similarities—in form and arrangement of their bones, etc.—are ascribed to the genetic relationship of all these animals, which is indicated by similarities in many other organs also (p. 196). On the other hand, the similarities between the legs of an arthropod and the legs of a vertebrate, or between the wings of an insect and the wings of a bird, are only in such characteristics as are absolutely essential to their similar functions, and which may therefore be reasonably supposed to have been evolved independently by natural selection. Thus it happens that, generally speaking, just those structural characters which are *least* important to the activities of the organism are *most* important for classification, *i.e.*, as indications of genetic relationships. This apparently paradoxical situation is readily understood when we realize that evolution—that is, *change* of the characteristics of organisms—is brought about by the natural selection of favorable mutations. For those characters which are most directly related to the organism's mode of life—that is, *adaptive* characters (p. 597)—are apt to be relatively *new* ones; whereas those characters of no direct adaptive significance are more apt to have persisted relatively unchanged for long ages. Thus, for instance, we find many differences in structure—*e.g.*, in the form of the limbs (Fig. 192)—among the different orders of mammals, obviously correlated with differences in their modes of life—terrestrial, arboreal, aerial, aquatic, etc.—some of these structures bearing superficial resemblances to those of other animals—birds, fishes, etc.—with similar modes of life. But we have no hesitation, nevertheless, in assigning all the mammals to one class, for we find innumerable points of resemblance among all of them—largely unrelated to any particular conditions of life—which indicate unmistakably that they are all more closely related to each other than any of them are to any other animals.

Summarizing: our inferences as to the common descent of two or more species (which can not be crossed) are based, not on resemblances in any one organ, but on the totality of the resemblances between these species, *especially* in such characters as are not directly related to their particular modes of life, because these resemblances may logically be supposed to represent the genes which they have in common by derivation from a common ancestor, while the differences between them are largely due to incorporation into the genetic constitution of each species of mutations favorable to it under its particular conditions of life.

Vestigial organs.—We have previously noted (p. 600) that by no means all the characteristics of any organism are adaptive, or useful. In particular, we find, in practically every kind of organism, useless organs which appear to be in a reduced and degenerate condition as compared with the homologous organs in other, more or less closely related, species. Such organs are called *vestigial.* More than a hundred vestigial organs have been listed in the human body; *e.g.*, the vermiform appendix, the tail-bones, etc.

(Fig. 65). Comparable numbers are found in other organisms, in proportion to the complexity of their structure and the care with which it has been studied. In general, whenever we find an organ which seems to be vestigial, we find, in some other, more or less closely related, species or group, an apparently homologous organ in a well-developed and useful condition. Vestigial organs are therefore presumed to represent the surviving vestiges, so to speak, of organs which were well-developed and functional in some ancestral species; or, to state the relation more strictly, the vestigial organ is a product of some of the genes involved in the production of a useful organ in the ancestral species, which have persisted unchanged while other genes, necessary to its full development, have been lost (*i.e.*, changed) by mutations. We find, by comparing related organisms, that it is a fairly general rule that organs which have become useless or unnecessary—as, for instance, by a change in the conditions of life—tend, in the course of evolution, to degenerate, *i.e.*, to become relatively smaller and less perfect in structure. For instance, animals of many kinds (crustaceans, fishes, amphibians, etc.), living in total darkness—*e.g.*, in subterranean caves—are blind, usually possessing quite useless vestigial eyes, which show, nevertheless, in each case, fundamental similarities of structure and development to the functional eyes of the most closely related daylight-inhabiting species. This evolutionary degeneration of useless organs is precisely what we should expect on the basis of mutation and natural selection. For, in the first place, random mutations are much more apt to decrease than to increase the size and perfection of any particular organ. If we study, in any particular organism (*e.g.*, Drosophila), all the mutations affecting any particular organ (*e.g.*, the eyes or the wings), we find that the great majority of such mutations effect decreases in the size, perfection of structure, and functional efficiency of this organ. This, as we have previously noted (p. 568), is to be expected *a priori*, since any random change in a complex mechanism is most apt to be detrimental. So long as the organ in question is necessary or useful to the organism, these detrimental mutations will be quickly eliminated by natural selection. But if the organ is useless or unnecessary, such mutations will tend, on chance, to accumulate in the course of generations, leading to the gradual degeneration, and perhaps the eventual complete disappearance, of this organ. This process will, moreover, probably be accelerated by natural selection. For useless organs must "compete," so to speak, with the useful organs of the body for the available food supply, and are, therefore, to some extent at least, actually detrimental to the organism. Moreover, vestigial organs are, in many cases—*e.g.*, the vermiform appendix—particularly liable to infection and disease, dangerous to the organism. For these reasons, natural selection will tend to accelerate the reduction and final elimination of such organs. It might be supposed, from these considerations, that, given sufficient time, all vestigial organs would be eliminated completely, as does undoubtedly occur in many cases. It must be remembered, however, as we have previously emphasized (p. 601), that natural selection acts on the *whole* organism rather than on any particular organ; its results, therefore, in respect to any particular organ, are likely to be very incomplete and imperfect.

If we find apparently homologous organs in two species, *A* and *B*,but better developed and more efficient in *A*, there are two possibilities: the condition in *A* may represent more nearly the ancestral condition of both species, this organ being vestigial in *B*; or the condition in *B* may represent a more primitive stage of evolution of this organ, which has become better developed, by the action of natural selection, in *A*. In practice, however, there is usually little difficulty in deciding between these alternative explanations in any particular case. For one thing, the relations of *A* and *B* to each other and to other species, as indicated by many other characteristics, will often answer the question with a considerable degree of probability. Aside from this, an organ in a primitive, relatively imperfect, stage of development is usually a quite different sort of thing from a vestigial, degenerating, organ. For an organ in successive evolutionary stages of increasing perfection must be useful *for some purpose* at each stage, in order to be preserved and improved by natural selection. An eye, for instance, is useful as a photo-receptive organ at every stage of its evolution, from the simplest "eye-spot" of photo-sensitive pigment through the various stages of development of focusing and adjusting mechanisms (p. 289), which increase its usefulness continuously. In many other cases, organs which at one stage of evolution serve one function are gradually altered, by the action of natural selection, to serve entirely different functions; as we have previously remarked, an organism is not like a machine intelligently designed to do certain things, but is a made-over, patched-up sort of an affair. At each stage, however, of the increasing perfection or alteration of function, the organ is useful to its possessor for something. It is quite otherwise with vestigial organs. If we examine, for instance, the vestigial eyes of blind cave-dwelling animals, we find, in most cases, some complex parts of the mechanism of a well-developed eye (of the type found in their daylight-inhabiting relatives), which are obviously quite useless because some other parts, absolutely essential to any visual function at all, are absent. Thus there is little danger of mistaking a vestigial eye for a primitive, relatively imperfect but nevertheless useful, type of eye.

There is another important difference between "progressive" and "retrogressive" evolution. The loss or great reduction of an organ, even a very complex one, need not necessarily be a gradual process; it may occur by a single mutation. Many cases are known of single mutations resulting in the almost or quite complete absence of organs such as wings or eyes. Such mutants may, perhaps, sometimes be preserved by natural selection under certain conditions. For instance, we often find, on small, windswept islands, wingless insects closely related to winged species of the nearest mainland. The advantage of their wingless condition, in this situation, is obvious: if they can not fly, they are much less apt to be blown out to sea and drowned. It is quite probable that, in many of these cases, the loss of the wings—or their reduction to a completely useless vestigial form—may have occurred by a single mutation, such as we know to be of fairly frequent occurrence in some insects (Fig. 159). The origin of a complex useful organ, however, in a race which has never previously possessed it, can not possibly, it seems safe to say, ever come about suddenly by a single mutation, but must be brought about by the gradual accumulation, by the action of natural selection, of numerous slight favorable mutations. Consequently we may expect to find more numerous and more nearly continuous stages in the evolutionary development of useful organs than in the reduction and loss of useless or unnecessary ones; which is, in general, what we do find by comparison of related organisms, living or extinct.

Developmental characters.—Frequently, though by no means always, related organisms resemble each other more closely in their early developmental stages than they do in their adult forms. The reasons for this are rather obvious. In the first place, the early stages are less complex, so far as their visible structure is concerned, so that there is less opportunity for visible differences to appear. Moreover, we have learned (p. 526) that the various genes determining the processes of development produce their phenotypic effects at different stages, some early, others later, in the course of development. This will, in general, be true of those genes which are different in two related species as well as of those which are identical. Any differences produced during early developmental stages, however, will usually automatically result in at least equal differences in later stages, since the later structures are, in general, derived directly from the earlier ones. In addition, the differences determined by later acting genes will be added to these earlier determined differences as development proceeds, so that the differences will tend to accumulate as the organisms develop. For these reasons, the genetic relationships of organisms are often much more apparent in their early developmental stages than later. In some cases, indeed, the study of embryonic stages exhibits unmistakably relationships which would scarcely be suspected from the structures of the adult organisms. This is particularly true of many parasitic or otherwise degenerate species, which have lost many of the characteristic structures of the group to which they belong. If the mutations responsible for these losses (or many of them) happen to produce their visible effects relatively late in development, the early embryonic stages may resemble fairly closely those of other, more typical, species of the same group. If these mutations (or most of them), however, produce their effects relatively early in development, there may be little or no indication, at any stage, of the genetic relationships of these aberrant species—as is, in fact, the case with some apparently degenerate organisms.

It is by no means always true that the early stages of related organisms resemble each other more closely than do the adult forms. The larvae of various kinds of insects, for instance, differ more strikingly from each other than do the adults of the same species. The same thing is true of some other animals which have very pronounced metamorphoses (p. 407). Again, the embryonic membranes (p. 403) of the higher vertebrates (reptiles, birds, and mammals) constitute a very great difference between these embryos and those of the lower vertebrates (fishes and amphibia), although in some other respects all these embryos exhibit marked resemblances. The very earliest stages of development, the cleavage stages (p. 394), may also differ so greatly in related forms—*e.g.*, in different classes of vertebrates—as to show absolutely no indication of relationship. In all these cases, obviously, some of the genes which are different in these related organisms produce visible effects early in the course of development. Many of these early differences involve special embryonic or larval structures, which have a direct adaptive relation to the special conditions of life of the embryo or larva; that is, they are relatively "new" characters evolved by natural selection for these stages under these conditions. Many of these special embryonic or larval structures are lost in the course of development; *i.e.*, they are either thrown off bodily (*e.g.*, embryonic membranes) or completely disintegrated (*e.g.*, many larval organs of insects, etc.). In such cases the adult structures are really derived from only a part of the embryo or larva, and may thus show no signs of some of the most striking specific differences characteristic of the early stages. In short, differences between related species may occur at any stage of development, embryonic, larval, or adult; it is therefore by no means a universal rule—though undoubtedly true in many cases—that genetic relationships are shown more clearly by early developmental characters than by adult structures.

In those cases in which the embryos of related organisms resemble each other more closely than do the adults, the higher—*i.e.*, more complex or specialized—species usually depart more widely, on the average, in their adult structures, from the embryonic forms than do the lower—*i.e.*, simpler or more primitive—species of the group. For this reason, the embryonic stages of higher organisms sometimes exhibit striking resemblances, in some respects, to the adult stages of lower species. Before the mechanisms of heredity and variation were understood, such facts were interpreted as meaning that the embryonic development of each individual (*ontogeny*) "recapitulates" the evolutionary history of its race (*phylogeny*). In terms of our present knowledge, this would mean that each new mutation produces a change which is added on to the *end* of the previous series of developmental changes. But this, as we have seen, is by no means always, or even usually, the case: mutations may effect changes at any stage of development. As we have already noted, there are, in fact, many embryonic and larval structures which are relatively "new" characters, in an evolutionary sense, and certainly have no relation to any adult structures of ancestral forms. The cases which were interpreted as "recapitulation" are simply those cases in which genes responsible for some of the adult structures of the higher species happen to produce their visible effects at relatively late developmental stages. For instance, the embryos of all vertebrates develop gill-slits in the sides of the pharynx at a certain stage of their development (Fig. 193). In the fishes these gill-slits later develop into functional gills (p. 223), but in the higher, air-breathing vertebrates they close up and disappear completely (except the first pair, which become the Eustachian tubes) before the completion of embryonic development. These gill-slits develop in the embryos of the higher vertebrates because the genes responsible for the development of gill-slits in the embryos of their fish ancestors have persisted unchanged, while the genes responsible for the closing up of these slits do not produce their visible effects until somewhat later. The gill-slits of the embryos of the higher vertebrates are really comparable to the gill-slits of the *embryo* fish, not to those of the adult fish. These embryonic gill-slits, in the higher vertebrates, are thus simply vestigial organs, which do no harm in the embryonic stage and have not been eliminated by natural selection. There are many similar cases, all of which can be interpreted as persistence of vestigial organs in the embryonic stages rather than as "recapitulation" of ancestral adult structures, and none which really justify the latter interpretation. The idea of "recapitulation" has therefore been generally discarded by modern biologists; this does not, of course, in any way lessen the value of these developmental characters as indications of genetic relationships.

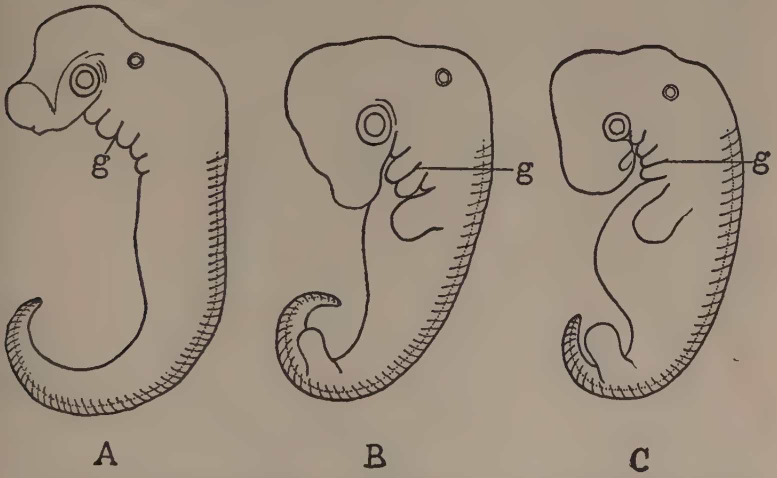


FIG. 193.—Vertebrate embryos: *A*, fish (shark); *B*, bird (fowl); *C*, mammal (man). *g*, gill-slits.

Chemical characters.—In comparatively recent years, it has been found that genetic relationships among organisms are clearly indicated not only by structural characters but also by characteristics of their chemical components, especially of their specific proteins. In general, we find in the corresponding tissues of closely related species either identical or very similar proteins, while more distantly related species show greater differences in this respect. Extensive studies of this kind have been made on the blood proteins of animals, by means of the extremely delicate tests called *immunity reactions*. If a foreign protein be injected into the blood of an animal, it causes the production in this animal of substances called *antibodies.* The foreign substance causing the antibody production is called an *antigen;* apparently only proteins act as antigens, and practically all[1] foreign proteins—*i.e.*, those not present naturally in the animal's own blood or tissues—do so. Despite a vast amount of study, very little is yet definitely known of the nature of antibodies, and practically nothing of how they are produced. Their presence in the blood is, however, easily detected by means of certain specific chemical reactions between each antibody and its antigen. These reactions are called *immunity reactions*, because some of them play an important part in immunity to infectious diseases. There are several types of immunity reactions; the one chiefly employed in studying "blood relationships" is the *precipitation test, i.e.*, the precipitation by each antibody of the specific antigen which produced it. If human blood serum, for instance, be injected into a rabbit, the blood of this rabbit, after several days, contains an antibody which, when mixed with human blood (outside the body), even in very minute amounts, produces a heavy precipitate; this is the most delicate test for human blood, serving to distinguish it from that of other animals. Similarly, if the blood of some other animal, instead of man, be used as the original antigen, the antibody produced in the rabbit reacts specifically with the blood of this particular animal. It is found, however, that although a prompt and strong precipitation is usually obtained only with the blood of the same species which furnished the original antigen, the blood of closely related species gives a slower and slighter precipitation. By using stronger solutions and allowing more time, the relationships of more distantly related species can be demonstrated in the same way. For instance, the reactions obtained with the bloods of apes closely resemble those obtained with human blood; the bloods of Old World monkeys come next, in their relationship to human blood; the bloods of American monkeys show slighter relationship to that of man, those of lemurs still less, etc. If sufficiently strong solutions be used and time enough be allowed, a relationship between the bloods of all mammals can be demonstrated. Similarly the bloods of all birds are shown to be related to each other, and less closely related to the bloods of reptiles; etc. The bloods of at least a thousand species of animals, representing several phyla, have been studied in this way. In general, the inferences as to the relationships of different kinds of animals from these blood tests agree with the conclusions previously drawn from the study of other kinds of characters—structural, developmental, etc. Of course, these "blood relationships" have, by themselves, no greater value in indicating genetic relationships than resemblances in any other kind of phenotypic characteristics; but the demonstration of these chemical relationships—discovered long after the theory of evolution had been generally accepted—constitutes one of the most striking confirmations of our general ideas of evolutionary relationships, based originally on entirely different kinds of characters. These chemical similarities between related species are due to the same cause as their structural and developmental similarities—the possession of some identical genes, derived unchanged from a common ancestor, which produce the same results in the metabolism and development of these different species.

---

[1] Gelatin seems to be the only exception.

In the last few years a very extensive series of studies has been made of immunity reactions similar in principle to those described above, using plant proteins as the antigens. From these studies has been deduced a system of genetic relationships covering the whole plant kingdom, coinciding very closely, in most cases, with those generally accepted on the basis of other kinds of evidence (p. 648). It is believed that the specific antigens involved in these reactions are the nucleoproteins of the plant tissues—that is, the substances constituting, or containing, the genes themselves (p. 512). If this interpretation is correct, this method may perhaps afford a means of demonstrating, with a high degree of probability, genetic similarities and differences between organisms which can not be crossed (p. 621).

Fossil remains of extinct organisms.—If all the kinds of organisms which have ever lived were alive today we should have every intermediate gradation between every species and every other one, and the relationships and lines of descent of all species would presumably be fairly clear.

This is, of course, far from being the case; the number of living species is probably but a small fraction of those which have become extinct in the course of evolution. We have, however, some remains of some of these extinct forms, which help to fill up some of the gaps between the living species and furnish fairly direct evidence of their evolutionary history. These remains, or *fossils*, comprise: the actual bodies, or parts of the bodies, of dead organisms which have been buried or surrounded by some sort of preserving material; petrified remains, in which the organic matter of dead organisms has been replaced, particle for particle, by mineral matter, often preserving even their microscopic structure with remarkable precision; impressions or molds formed in mud which has subsequently become rock; and casts produced by the later filling of such molds by mineral matter, preserving, of course, only the external form of the organisms. Fossils are found chiefly in *sedimentary rocks*, *i.e.*, rocks formed by the slow deposition in water of sand, clay, mud, or lime, which subsequently hardens under pressure into rock. To a smaller extent, fossils are found embedded in dust or sand drifts, asphalt, amber (a kind of petrified resin), and even in ice (in arctic regions).

On the whole, fossil remains furnish only an extremely fragmentary record of the life of the past. This is not surprising when we consider the peculiar concatenation of circumstances necessary for the formation, preservation, and discovery of fossils. In the great majority of cases, only hard parts of organisms—shells, bones, wood, etc.—are preserved as fossils; of the vast multitude of lower organisms with no such skeletal structures only very few, and usually very imperfect, traces are ever found. Again, since fossils are found, for the most part, only in sedimentary rocks, the great majority of them represent aquatic, chiefly marine, organisms; terrestrial species are, generally speaking, poorly represented. Sedimentary rocks are formed only under certain conditions; namely, relatively near the shore, where a considerable amount of sediment is being deposited, on areas which are *sinking*, so that a considerable thickness of sediment can accumulate. If these sedimentary rocks later become very deeply buried, they are usually distorted and disintegrated (*metamorphosed*), by heat and pressure, and their fossils largely or entirely destroyed. If, on the other hand, they are later raised above the surface of the water, and remain thus exposed for a long time, they are largely *eroded* by the atmosphere and running water, and again their fossils are largely destroyed. Finally, those fossils which have escaped these various vicissitudes of the ages can only be discovered by us if they happen to lie, at present, at or near the surface of the ground, in accessible parts of the earth. Considering all these factors, the surprising thing is not the incompleteness of the fossil record, but rather how much of it has been preserved and discovered. Since the time of Darwin—who emphasized the almost hopeless incompleteness of the fossil record—enormous advances have been made in the discovery and study of fossils, and this study (*paleontology*) has added very greatly to our knowledge of the evolutionary history of existing species, filling in many of the "missing links" in their ancestry.

Sedimentary rocks, because of their method of formation, form successive layers, or strata, the later (newer) layers lying on top of the earlier (older) ones. By comparison of these strata in all parts of the earth, all the sedimentary rocks of the earth can be arranged in a temporal series, from oldest to most recent. There are, however, considerable gaps between some of these strata, because the intervening layers have not yet been found in any accessible part of the earth's present surface. The strata are divided, by these gaps, into divisions and subdivisions called *eras* and *periods* (Fig. 194). As the study of the strata progresses and is extended to ever wider regions of the earth, many of the gaps are filled up and the lines of demarcation between these divisions consequently become less clearly marked. The *relative* durations of the different periods can be fairly well estimated by the thickness of the strata, but there has been, until very recently, no reliable method of estimating their *absolute* durations, so that there have been great discrepancies between different estimates. Some estimates made by physicists, based on assumptions now known to be entirely wrong, were absurdly low. The estimates of geologists, based on calculated rates of deposition of sediment, have been, in general, greater, but have differed considerably among themselves, because the rates of deposition vary enormously under different conditions and it is very difficult to estimate an "average" rate. The estimates of biologists, based on apparent rates of evolutionary changes of organisms, have usually been still greater. Recently a probably highly reliable and fairly accurate method of determining the ages of rocks, based on the rates of transformation of radio-active elements, has been employed. This method, which is undoubtedly more trustworthy than any of the others, shows the durations of the geological periods to be much greater than most previous estimates, and strongly confirms our ideas of the slowness of evolutionary changes. This evidence indicates the time from the beginning of the Paleozoic era to the present as about 750,000,000 years, the duration of the Proterozoic era as probably greater than this, and the duration of the Archeozoic era as probably greater than the sum of all the others (Fig. 194). We can therefore assert with a considerable degree of confidence that life has existed on the earth for at least a billion years, and probably much longer.

The fossils found in the most recent strata resemble the organisms now living, belonging to the same or closely related species. As we go further back—*i.e.*, to earlier strata—the fossils differ more widely from the present organisms, the representatives of each group are, on the whole, more primitive—*i.e.*, simpler or less specialized—and we find intermediate types connecting many of the present groups with each other. As we go further back, however, we find the rocks more metamorphosed (p. 637), the fossils therefore fewer and less well preserved, and the record of evolution consequently more incomplete and more difficult to interpret. The accompanying diagram (Fig. 194) shows roughly the history of the main groups of organisms, as indicated by the fossil remains now known. In the oldest (Archeozoic) sedimentary rocks, there are no recognizable fossils; there is, however, indirect evidence of the existence of some form of life, for these rocks contain *graphite* (a form of free carbon) and *limestone*, minerals which, so far as we know, are produced only as results of the life processes of organisms. In the Proterozoic rocks

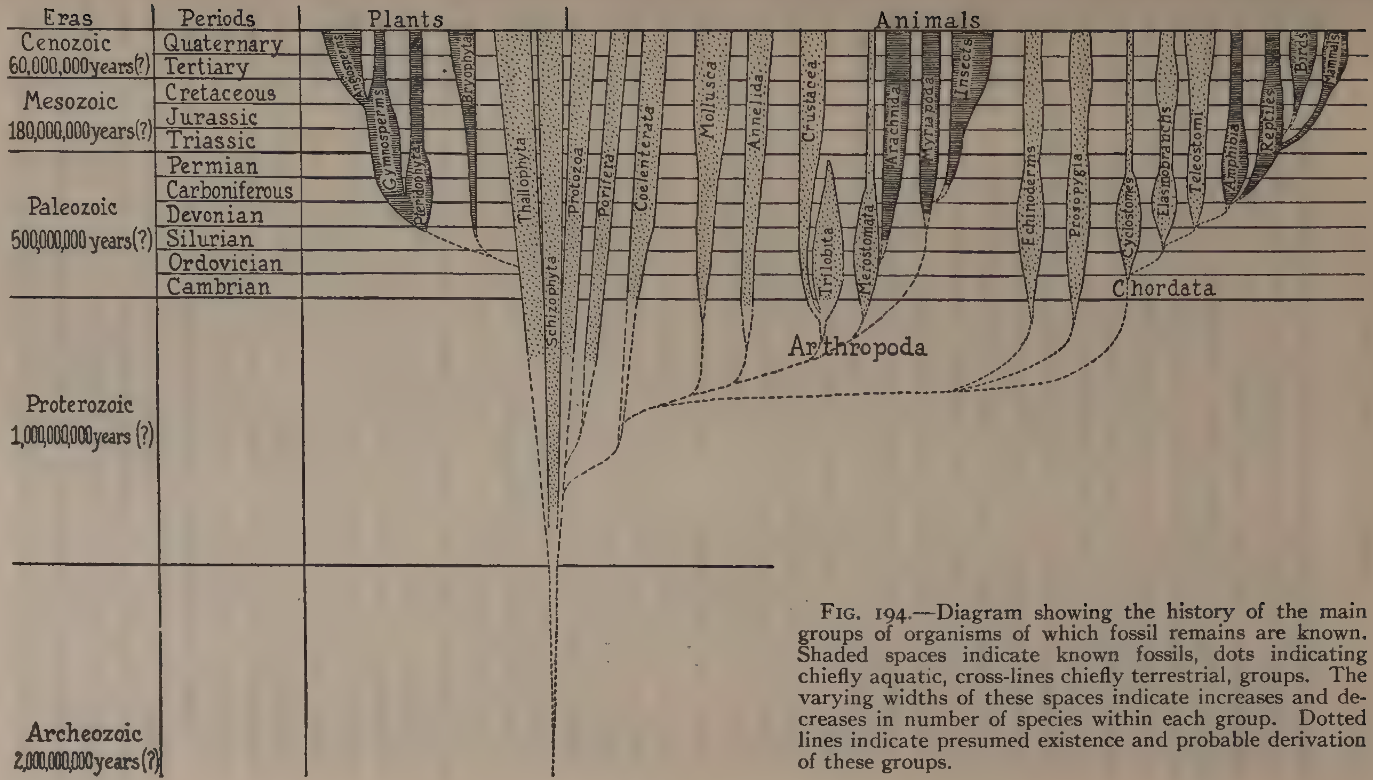


FIG. 194.—Diagram showing the history of the main groups of organisms of which fossil remains are known. Shaded spaces indicate known fossils, dots indicating chiefly aquatic, cross-lines chiefly terrestrial, groups. The varying widths of these spaces indicate increases and decreases in number of species within each group. Dotted lines indicate presumed existence and probable derivation of these groups.

fossils are still very scarce and, for the most part, poorly preserved, but some recognizable ones are found. The oldest recognizable fossils belong to the Schizophyta, the group which comprises the simplest living organisms, bacteria and blue-green algae (p. 36). In the upper strata of the Proterozoic era are found unmistakable fossil remains of algae, protozoa, and sponges, tracks and burrows which seem to have been made by some kind of "worms," and, near the very top of these strata, a few fossils of other invertebrate groups. The Proterozoic rocks are, however, for the most part, badly metamorphosed, and at the top of this series—between the upper Proterozoic and lowest Paleozoic strata—there is a considerable gap; *i.e.*, none of the sedimentary rocks formed during this interval have yet been found at the present surface of accessible parts of the earth. The geological evidence shows, in fact, that most of the present land areas of the earth were also land areas during the latter part of the Proterozoic era, so that most of the previously formed sedimentary rocks were greatly eroded at that time. The oldest good fossiliferous rocks are those of the Cambrian period; here we find abundant fossils of algae and of all the principal phyla of invertebrates, but no vertebrates, no plants higher than thallophytes, and *no terrestrial organisms* of any kind—all life, apparently, was still aquatic. The animals, though belonging to the same phyla as those of today, were, in general, very different and, on the whole, much more primitive than the present species; many of them belonged to classes or subclasses which are now extinct or nearly so, *e.g.*, the Trilobita, Merostomata, etc. (Fig. 194). Later periods of the Paleozoic era furnish fossils of the lower classes of vertebrates and of various kinds of terrestrial plants and animals, as indicated in the diagram. The Mesozoic and Cenozoic eras show the rise of the classes of organisms now most abundant: angiosperms, insects, the higher vertebrates, etc.

These fossil remains thus show us a good deal of the evolutionary history of the various groups of organisms. This record, as will be apparent from our diagram, is far from complete. It does not, for instance, show us the direct connections between any of the different phyla of animals. This is due to two causes: the strata of the Proterozoic era, during which most of these phyla presumably first evolved, are either still unknown or are too extensively metamorphosed to yield recognizable fossils; and the simplest representatives of all these phyla are soft-bodied, worm-like animals which could leave no remains capable of being preserved as identifiable fossils. Similarly, the connections of the higher plants with the thallophytes are not shown by the fossil record, the intermediate forms—such as the bryophytes—being soft, non-woody plants. The connection between pteridophytes and spermatophytes, however, is very completely shown; it is, in fact, impossible to draw the line between these two phyla among the Paleozoic fossil plants; the connections between the various classes of these two phyla are also, for the most part, well shown. Within each phylum of animals, also, the connections between the various classes are, in some cases, clearly shown by the fossil remains of intermediate forms. This is especially true of the vertebrates, because their evolution has taken place relatively recently, most of them have bony skeletons capable of preservation as fossils, and they have been more extensively studied than any other group. The mammals and reptiles are very completely connected by fossil remains of intermediate forms; the connections between birds and reptiles, and between reptiles and amphibia, are only a little less complete; and the gap between amphibia and fishes is partly bridged. At the lower end of the vertebrate group, however, there is another great gap in the fossil record: the simplest Chordata (p. 649) are soft-bodied, worm-like animals, incapable of leaving fossil remains, or, at least, any which would be distinguishable from those of other "worms."

Within smaller groups, the fossil record shows, in many cases, very complete series of intermediate forms connecting species or groups now very distinct, and showing clearly the lines of evolution of highly specialized types—such as horses, camels, elephants, etc.—from primitive ancestors. It is obvious, of course, that fossil series, however complete, can not actually prove that any particular species is the descendant of some particular earlier species or the ancestor of some particular later one. When we find, however, as we often do, a series of fossils differing from each other by "steps" no greater than the differences between closely related species or even varieties, and occurring in the proper order in successive geological strata, the presumption is certainly very strong that this series represents, at least approximately, the line of evolution of the group.

Geographical distribution of organisms.—We have noted, in the preceding chapter (p. 612), the important part which geographical factors play in evolution; we should expect, therefore, to find the evolutionary history of organisms clearly reflected in the geographical distribution of species and groups, both living and extinct. It is a familiar fact that no species is found uniformly distributed over the earth. There are, in general, two groups of factors determining the distribution of any particular species. One group consists of *ecological* factors, *i.e.*, present environmental conditions which determine the possibility of the organism living in any particular place; *e.g.*, some organisms live in water, others on land, some in warm climates, others in cool climates, etc. There are, of course, in addition to such very obvious ones, many other more subtle environmental factors affecting the distribution of an organism: not only physical and chemical conditions of its non-living environment, but also—and, on the whole, even more important—the distribution of other organisms, which furnish its food, prey on or parasitize it, compete with it, etc. (p. 594). All these ecological factors together, however, do not entirely account for the actual distribution of organisms, for, in general, no species is found in all regions of the earth where it could live successfully. This is proved by numerous cases in which organisms—both plants and animals—transported by human agency, either intentionally or accidentally, to new regions, not only survive but often flourish better than in their original habitats and supplant native species. In general, similar environmental situations in different parts of the earth are occupied by different species, often by species belonging to entirely different groups. The actual geographical distribution of organisms can be explained only by taking into account, in addition to present ecological factors, *historical* factors, *i.e.*, the evolutionary history of the species or group.

We usually find the most closely related species neither in the same territory nor in very distant parts of the earth, but in neighboring regions separated from each other by some kind of geographical barrier preventing their intermingling; this is, of course, exactly what we should expect from the rôle which geographical barriers play in the origin of species (p. 612). In those cases in which the most closely related living species of a group are found in very distant parts of the earth, evidence furnished by fossils usually shows that these species are the surviving remnants of a group which formerly had a wider distribution including the intermediate regions. The distribution of any particular group—genus, family, etc.—comprising either living or extinct species or both, usually clearly indicates a definite *center of dispersal* at or near which the group originated and from which it has spread more or less widely, and with more or less evolutionary changes, in various directions. As we have noted previously (p. 612), large continuous areas, such as oceans or continents, uninterrupted by any barriers to the dispersal of organisms of a particular group, are often found to be inhabitated throughout by the same species—with, perhaps, local varieties, not very definitely demarcated—while isolated neighboring regions usually contain distinct, though closely related, species. This is very clearly shown in the flora and fauna of islands separated by a considerable distance from the mainland. The species of plants and animals found on such islands are always most closely related to those of the nearest continent; but a large proportion of them are specifically distinct, except in groups such as strong-flying birds which can easily pass from the mainland to the islands. The proportion of distinct species in each case is clearly related to the age of the islands, their distance from the nearest mainland and the length of time they have been separated from it (as shown by geological evidence), and to the facilities for migration of each group of organisms. Similar facts are found in isolated mountain valleys, inland waters, etc. All these facts are, of course, exactly what we should expect from what we have learned of the rôle of geographical isolation in species formation. In isolated islands and inland waters we often find, too, the surviving species of primitive, formerly much larger and more widely distributed, groups, which have here escaped the competition of more modern and efficient organisms which has exterminated them elsewhere.

The geographical distributions of different groups of organisms are, of course, quite different, the distribution of each group depending upon its age, in relation to the various geographical changes of the earth's surface during different geological periods, and upon its means of dispersal. The accompanying zoo-geographical map of the earth (Fig. 195) is based primarily on the distribution of terrestrial mammals, though it applies also fairly well to some other groups of animals. Each *zoo-geographical region* is characterized by the presence of certain groups (genera, families, etc.) and the absence of certain others. Some groups are confined exclusively to one region, though many, of course, extend over more than one, and the boundaries between adjacent regions are never absolutely sharply marked. It will be evident, by inspection of this map, that the faunal differences between these regions are determined in part by ecological, especially climatic, factors; thus the differences between the northern and the southern regions of each hemisphere are obviously correlated with temperature. This, however, is but a small part of the story, for the faunal differences between the several southern regions are, in general, greater than the differences between any one of them and its immediately adjacent northern region; again, the animals of the temperate southern parts of each southern region are, on the whole, most closely related to those of the tropical parts of the same region rather than to those of the temperate parts of other regions. The regions are separated from each other by more or less effective barriers—water, mountains (*e.g.*, the Himalayas), or deserts (*e.g.*, the Sahara). The boundaries of these regions and the faunal resemblances and differences between them can, however, be completely explained only by taking into account the geographical changes of the earth's surface during past geological periods and the evolutionary history of their animals (more especially the mammals) during these periods.

The closest faunal resemblance between any two of these

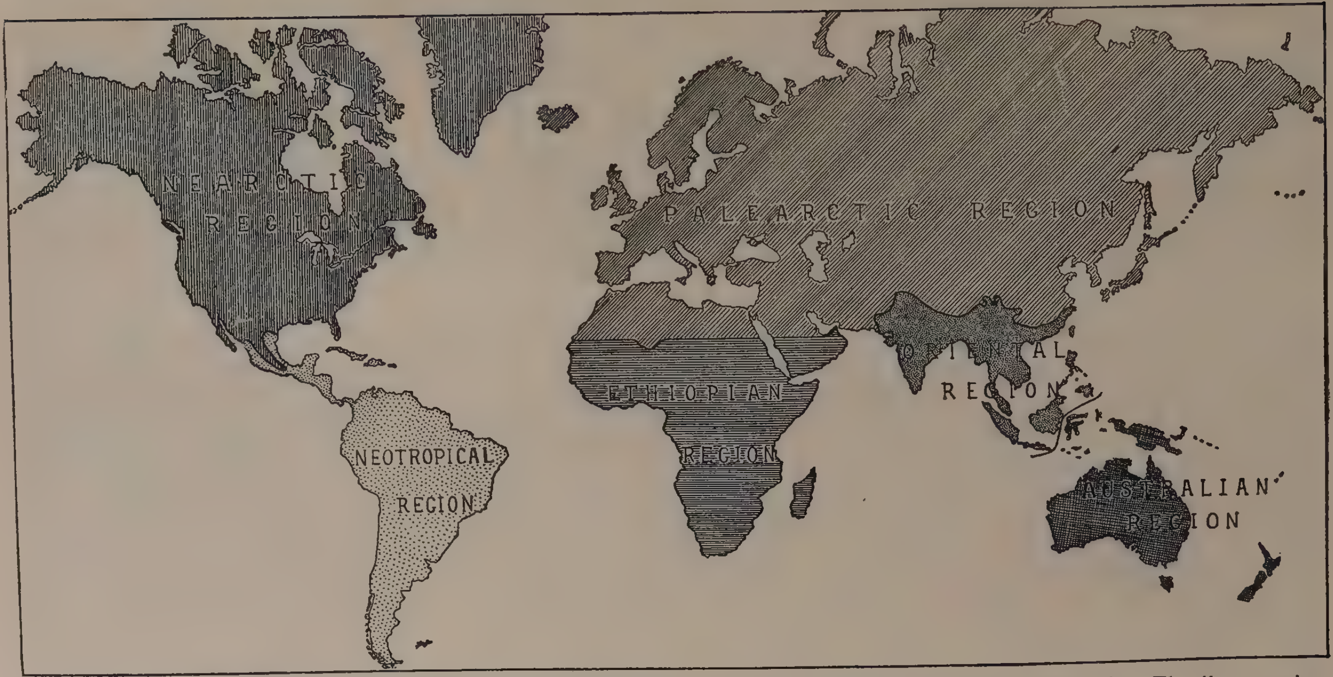

NEARCTIC REGION
PALEARCTIC REGION
ORIENTAL REGION
ETHIOPIAN REGION
NEOTROPICAL REGION
AUSTRALIAN REGION

FIG. 195.—Zoo-geographical map of the earth, based primarily on the distribution of terrestrial mammals. The line running through the East Indies, separating the Oriental and Australian regions, is called *Wallace's line*.

regions is between the Palearctic and Nearctic regions. These two regions are now completely separated by water, and also by the almost uninhabitable arctic areas. But geological evidence shows that they have been connected by extensive land bridges, and also that the climate of the now frigid arctic lands was temperate or even sub-tropical, thus permitting free intermigration between the two regions, in relatively recent times.

On the other hand, the Australian region is the most distinct of all; the sharpest of all zoo-geographical boundaries is *Wallace's line*, passing between rather closely adjacent islands—only 20 miles apart in one place—of the East Indies (see Fig. 195). Geological evidence shows that this region has been separated from the rest of the earth by water continuously since the beginning of the Cenozoic era or even earlier. The most striking faunal peculiarity of this region is its almost exclusive possession of the two most primitive groups of mammals, the monotremes and marsupials (pp. 402, 406), and the almost complete absence of higher (placental) mammals. Fossil remains prove that these primitive types of mammals were formerly widely distributed over the earth, but have since become extinct elsewhere (except the opossums in America), being unable to compete successfully with the higher types. But the higher mammals originated *after* the Australian region had become separated from the rest of the earth by water, and consequently never reached this region (except for a few "accidental" arrivals much later). Consequently the marsupials (and a few species of monotremes) have been able to survive and flourish in this region, in the absence of more efficient competitors. But when placental mammals—*e.g.*, rabbits, pigs, etc.—have been introduced, by human agency, they have spread and multiplied enormously, at the expense of the native marsupials.

Next to the Australian region, the Neotropical region is the most distinct. The northern boundary of this region is not marked, at present, by any very definite barrier, but South America was separated from North America by water during much of the Tertiary period, which accounts for the distinctness of its present fauna. This region is at present the chief home of the Edentata, the most primitive order of placental mammals, and fossil remains show that it has long been so.

The Ethiopian and Oriental regions have been continuously connected with the Palearctic region throughout recent geological periods, and their faunas are therefore, on the whole, less different from that of the Palearctic region and from each other than the Neotropical fauna is from the Nearctic. Many of the animals now confined to these regions were formerly widely distributed over the Palearctic region, but have been driven southward by decreasing temperatures during the most recent (Quaternary) period.

The present geographical distributions of other groups of organisms—aquatic as well as terrestrial—can similarly be explained by taking account of their evolutionary history and the accompanying geographical changes of the earth's surface.

Phylogeny.—By means of the several kinds of evidence discussed in the preceding pages, we can reconstruct, with some degree of probability, the *phylogenies*—*i.e.*, the evolutionary histories or lines of descent—of the various groups of organisms. There is, of course, no way of actually proving the correctness of these hypothetical phylogenies, since they deal with things which have happened in the past and are therefore not susceptible to experimental proof; it is merely a question of a balance of probabilities yielded by the various available kinds of indirect evidence. The fundamental assumption is that *genetic similarity* implies *common descent; i.e.*, the more genes two kinds of organisms have in common the more closely they are related by descent. But we have, at present, no general method of directly proving the genetic relationship of different species or groups of organisms, since the only method yet known of proving genetic relationship is by breeding tests, which are usually possible only within a species or between very closely related species (p. 609). We can, therefore, in general, only infer genetic relationships from phenotypic resemblances and geological and geographical distributions. The most satisfactory of these indirect kinds of evidence is that of fossil remains, for these show not only the structural resemblances between species and groups but also their temporal succession. But this kind of evidence is, as we have seen, very incomplete and fragmentary; in its absence we must resort to still more indirect kinds of evidence, such as structural, developmental, and chemical resemblances and geographical distributions of living species. In general, the more distantly related organisms—that is, the larger groups—we deal with, the greater are the uncertainties of their relationships and phylogenies. The phylogenetic relationships of the different phyla are little more than "guesses"; we can only say that some guesses are more

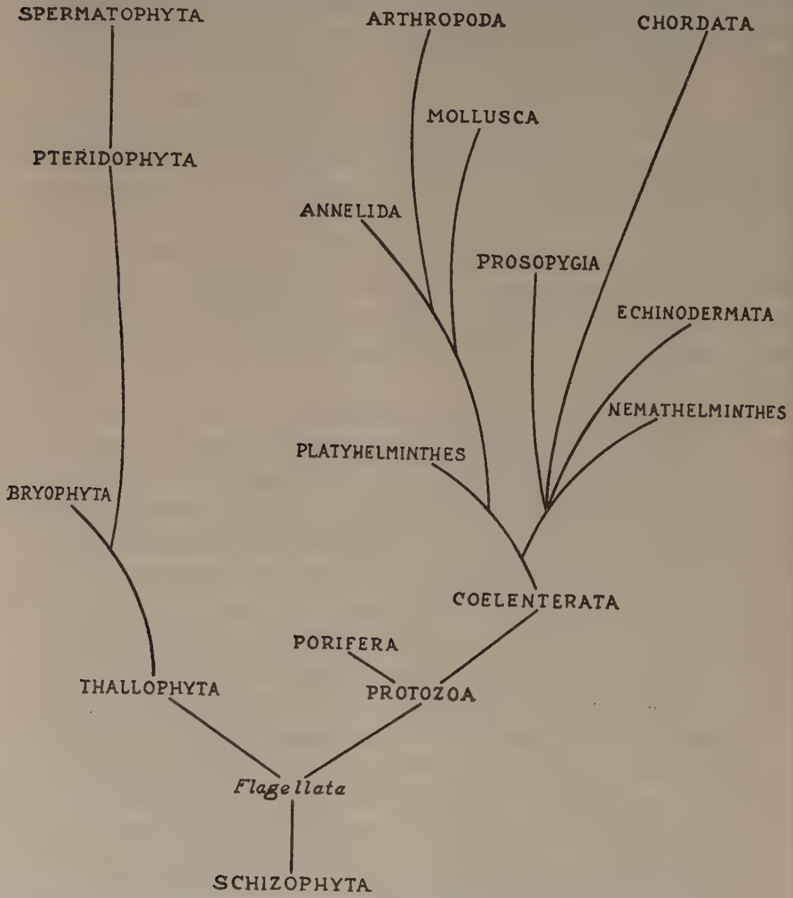

SPERMATOPHYTA
ARTHROPODA
CHORDATA
MOLLUSCA
PTERIDOPHYTA
ANNELIDA
PROSOPYGIA
ECHINODERMATA
NEMATHELMINTHES
PLATYHELMINTHES
BRYOPHYTA
COELENTERATA
PORIFERA
THALLOPHYTA
PROTOZOA
Flagellata
SCHIZOPHYTA

FIG. 196.—Diagram showing probable phylogenetic relations of the main groups of organisms (these groups are defined in Appendix I).

probable than others. The accompanying diagram (Fig. 196) represents one such guess—probably as good a one as any. As we have seen (p. 640), fossil remains afford us little help here, except by indicating that some groups are older than others—the simpler ones, according to all the available evidence, older than the more complex. The only direct connection between phyla shown by fossil remains is that between the Pteridophyta and Spermatophyta (p. 641). The only phyla completely connected by intermediate living forms are the Protozoa and Thallophyta, and probably, though less clearly, the Schizophyta. All the other connections shown in the diagram are based simply on structural and development resemblances—usually not very close—between the species, or some of the species—especially the more primitive ones—of different phyla. Some of these connections are generally accepted as being the only probable ones; there is very little difference of opinion as to the interrelations, as here shown, of the phyla of plants and of the lower phyla (up to Coelenterata) of animals. On the interrelations of the higher animal phyla, however, there is no general agreement at all, except that they are all derived from the Coelenterata. The scheme given here is based chiefly on the method of development of the mesoderm and coelom in these different phyla (p. 396); as to the significance of this in indicating phylogenetic relationships there are wide differences of opinion—and no way to decide.

One of the most hotly contested questions of phylogeny has been that of the origin of the vertebrates. As we have previously noted (p. 641), fossil remains throw no light on this question; although the first vertebrates appear after the Cambrian period (Fig. 194), there are no earlier fossils showing any connection between vertebrates and invertebrates. This gap is, however, partially bridged by certain living animals, of kinds which would be very unlikely to leave any recognizable fossil remains. These animals are included with the vertebrates in the phylum Chordata. Of these lower chordates, the Cephalochorda (lancelets) are most closely related to the vertebrates, showing many of the typical vertebrate characteristics of structure and development, though much simpler than any true vertebrate; they are generally regarded as probably resembling fairly closely, in most respects, the primitive ancestors of the vertebrates. The Urochorda (tunicates) are mostly sessile animals, which show little or no resemblance to vertebrates in their adult forms, but their embryonic development and larval forms show so many typical vertebrate characteristics that they are generally regarded as degenerate descendants of primitive vertebrate-like ancestors, perhaps related to the Cephalochorda. The Hemichorda are much more doubtfully related to the vertebrates; they are marine "worms," some of which (especially Balanoglossus and related genera) have gill-slits and structures which are supposed to represent a notochord and a dorsal hollow nerve cord, and therefore may be descended from ancestors of the vertebrates still more primitive than those represented by the Cephalochorda. The acceptance of these animals as representing, to some extent at least, the ancestors of the vertebrates leads to the view that this phylum was derived from some very low worm-like invertebrates, rather than from any of the higher invertebrate phyla. In the Hemichorda and Cephalochorda especially, and also, though less clearly, in some of the lower vertebrates, the mesoderm and coelom are developed from pouches of the enteron, as in the Echinodermata (Fig. 130), some of the Prosopygia, and the Chaetognatha (commonly placed in the phylum Nemathelminthes). For this reason, these three phyla are regarded by some as more closely related to the Chordata than the other invertebrate phyla (see Fig. 196). This evidence, weak as it is—if, indeed, it be significant evidence at all—is the only clew we have as to the origin of the vertebrates and their relationships to other phyla.

Within the group of vertebrates proper (subphylum Vertebrata), the several classes, and many of the smaller groups (orders, families, etc.), are fairly well connected by fossil remains of intermediate forms (p. 641). These fossils consist, for the most part, of skeletons only, but since there are characteristic skeletal differences closely correlated with the other, more important, differences between the living classes and orders, these remains permit us to trace their phylogenetic relationships with a considerable degree of probability. These relationships are shown

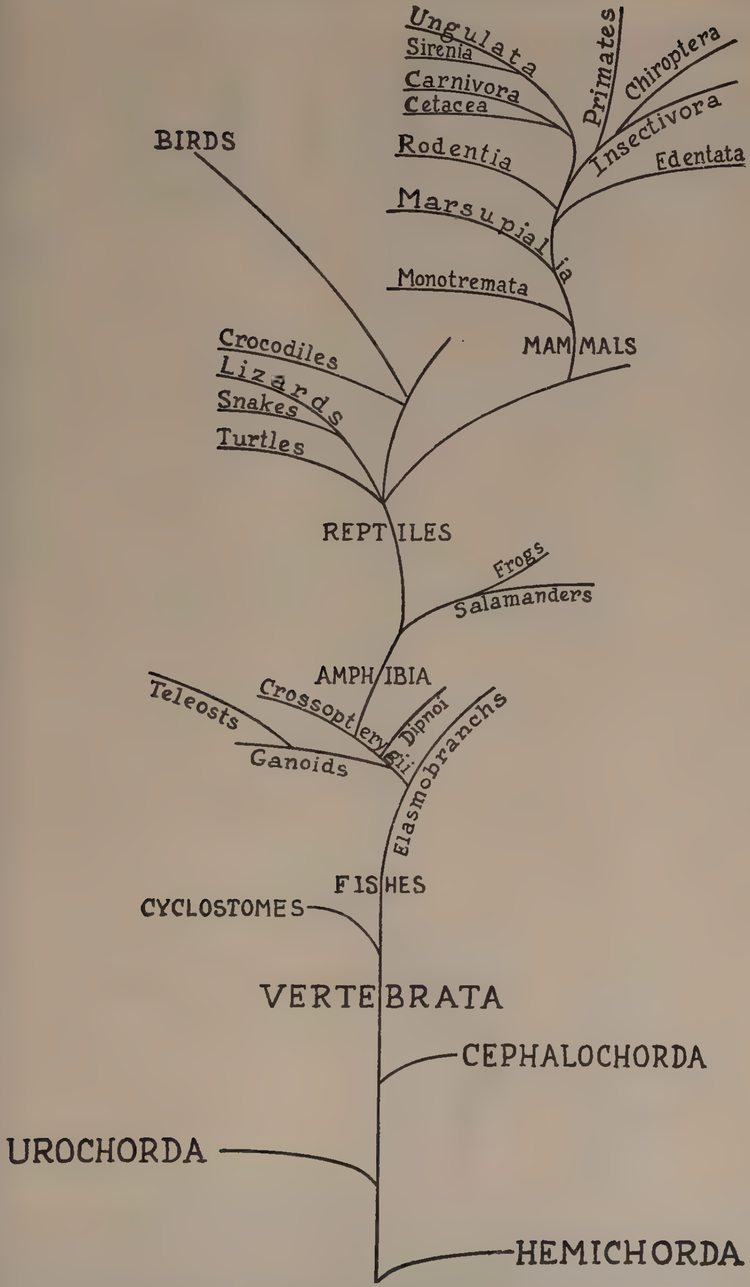

Ungulata
Sirenia
Carnivora
Cetacea
Primates
Chiroptera
Insectivora
Edentata
Rodentia
Marsupialia
Monotremata
BIRDS
MAMMALS
Crocodiles
Lizards
Snakes
Turtles
REPTILES
Frogs
Salamanders
AMPHIBIA
Teleosts
Crossopterygii
Dipnoi
Elasmobranchs
Ganoids
FISHES
CYCLOSTOMES
VERTEBRATA
CEPHALOCHORDA
UROCHORDA
HEMICHORDA

FIG. 197.—Diagram showing probable phylogenetic interrelations of the chordates (the groups are defined in Appendix I).

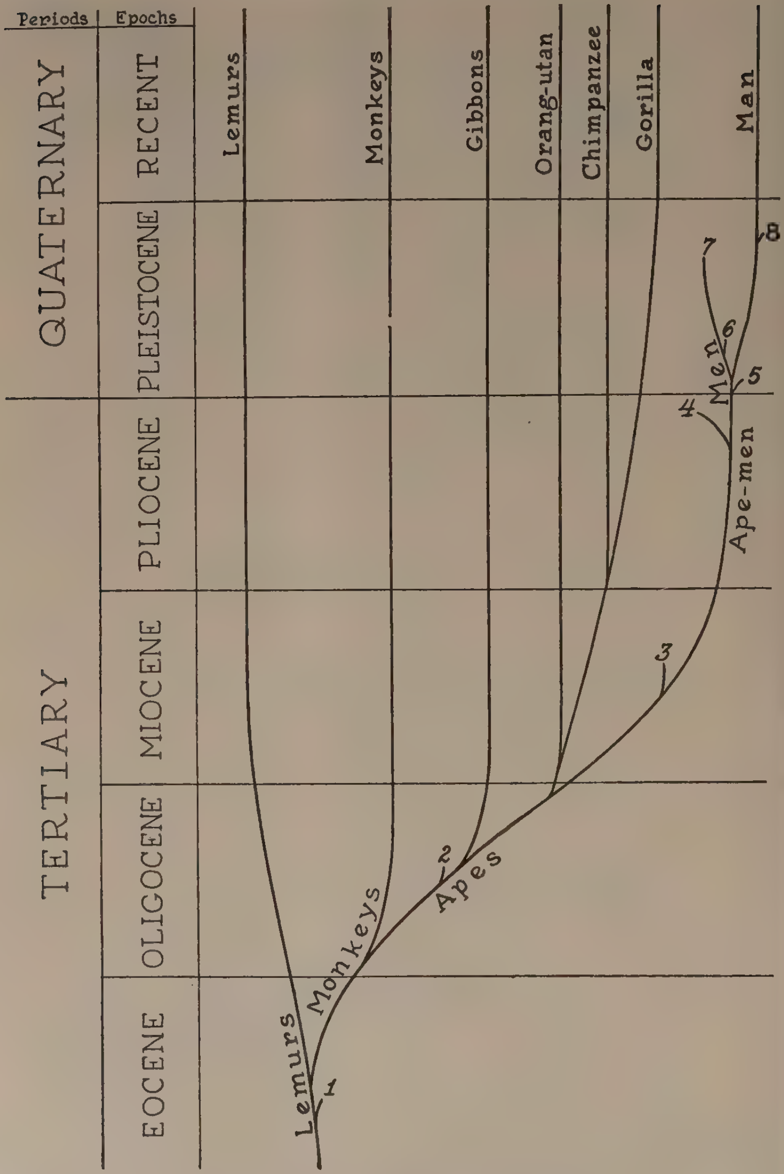

Periods
Epochs
QUATERNARY
TERTIARY
RECENT
PLEISTOCENE
PLIOCENE
MIOCENE
OLIGOCENE
EOCENE
Lemurs
Monkeys
Gibbons
Orang-utan
Chimpanzee
Gorilla
Man
8
7
6
5
Men
4
Ape-men
3
Apes
2
Monkeys
Lemurs
1

FIG. 198.—Diagram showing probable phylogenetic interrelations of the primates, and the fossil forms which probably represent most closely the line of human ancestry: *1*, *Notharctus*, a primitive lemuroid primate; *2*, *Propliopithecus*, a primitive ape; *3*, *Dryopithecus*, a somewhat man-like ape; *4*, *Pithecanthropus*, the "ape-man"; *5*, *Eoanthropus*, the "dawn man"; *6*, *Homo heidelbergensis; 7*, *Homo neanderthalensis;* 8, oldest fossil remains of *Homo sapiens.*

diagrammatically in Fig. 197; the geological ages of the main groups are shown in Fig. 194.

The fossil evidence of the descent of man is not quite so complete as that of some other mammals (*e.g.*, the horse, elephant, and camel), because the habitats and modes of life of primates are such that their remains are unlikely to be preserved as fossils; but there are sufficient remains of "missing links" to show fairly clearly the phylogenetic derivation of man from the apes and of these from the lower primates. In Fig. 198 are shown the phylogenetic interrelationships of the primates, especially those most closely related to man, and the geological ages of the fossil forms believed to represent most closely the line of human ancestry. It is impossible to draw a sharp line, among these fossil forms, between apes and men. In the Pleistocene epoch there are, as shown in the figure, several distinct species of "men," using this word in a broad sense. All human races now living belong to a single species, *Homo sapiens*, the oldest fossil remains of which are found in the latest Pleistocene strata, probably about 50,000 to 100,000 years old.

CHAPTER XXVII

THE ORIGIN AND NATURE OF LIFE

The various lines of evidence considered in the preceding chapters make it seem probable, at least, that all existing organisms have been derived, by mutations and the action of natural selection, from one or a few simple forms of life. This raises a still more fundamental question: how did these simplest living things originate? It seems quite certain (regardless of which of the several theories of the origin of the earth we may accept) that conditions on the earth were at some time—probably some billions of years ago—absolutely incompatible with the existence of life in any form. It seems almost equally certain that no living thing can have reached the earth from any other body, as the conditions and vast dimensions of interplanetary space seem to preclude any possibility of the transportation of life across it. This leaves us with the highly probable conclusion that living things have originated, somewhere on the earth, at some time within the past few billion years, from non-living matter. Any consideration of how this has occurred must necessarily, at present, be largely speculative, as no one has yet observed, under either natural or experimental conditions, the origin of any living thing except from already living matter. In recent years, however, two lines of evidence have thrown considerable light on this problem—at least to the extent of more accurately defining the problem, which is certainly a necessary first step toward its solution. These two lines of evidence are: on the one hand, the discovery of living things much simpler than any previously known; and, on the other hand, the evidence from the study of heredity and mutation indicating the gene as the essential basis of life.

The simplest living things.—We have learned that all the larger, macroscopic, organisms are made up of numerous protoplasmic units, or cells, each of which has all the general properties characteristic of life, and which can, under suitable conditions, continue to live indefinitely outside the body of the organism. Each multicellular organism, moreover, begins its individual life as a single cell, which gives rise, by a continuous series of divisions, to all the cells comprising the organism. The non-cellular components of the organism—blood plasma, bone, shells, etc.—are produced by the cells, and none of these materials display the phenomena of life apart from the cells. In short, the *life* of the organism is the life of its component cells. We have learned, also, that there are, below the limit of naked-eye visibility, numerous kinds of microscopic organisms, each of which consists of a single cell, having all the general characteristics of life displayed by the more familiar larger organisms. There is, moreover, every reason to believe that unicellular organisms existed long before multicellular ones and have given rise to the latter by processes similar to those we see operating today—variation and selection—continued through long ages.

The typical unicellular organisms, however, are already highly complex structures, differentiated into cytoplasm and nucleus, with a complex mechanism of nuclear division, and usually with other specialized "cell organs," such as plastids, contractile vacuoles, cell walls or membranes, flagella, etc. It is inconceivable that such complex mechanisms could originate at one jump from non-living substances, however complex chemically. In fact, all our experience shows that these unicellular organisms originate only in the same way that higher organisms do—from previously living organisms of the same, or nearly the same, kind. It has long been recognized that we must look for the origin of life in something much simpler than the typical, quite complex, unicellular organisms. It was formerly supposed that these still simpler forms of life should consist of "protoplasm"—*i.e.*, cytoplasm—without a nucleus, and the supposed discovery of such non-nucleate organisms was occasionally reported; all such discoveries were, however, subsequently found to be erroneous. We now realize that this search was in the wrong direction, for it is the nucleus which is essential to life, the cytoplasm which is incidental—in the same sense that, in a multicellular organism, the cells are essential, the intercellular materials incidental. If there are living things simpler than the typical unicellular organisms with distinct nucleus and cytoplasm, we should rather expect them to be more comparable to nuclei without cytoplasm. Such organisms are, in fact, numerous and well known—the bacteria. These organisms contain, as shown both by staining and by chemical analysis, a large proportion (much larger than in typical cells) of the characteristic nuclear material, chromatin or nucleoprotein, distributed more or less throughout the cell (Fig. 10, *A*), without any chromatin-free region comparable to the cytoplasm of typical cells. There is, therefore, no logical reason why they should not be regarded as nuclei without cytoplasm. In their nearest relatives, the Cyanophyceae (blue-green algae), we find a series of stages in the differentiation of nucleus and cytoplasm—that is, the segregation of the chromatin in one region of the cell (Fig. 10, *B–D*)—accompanied by increase in the size of the cell as a whole, indicating that the cytoplasm is something added on, so to speak. The smallest visible bacteria, lying at the extreme limit of microscopic visibility (Fig. 4, *F*), resemble, in size, staining properties, and microscopic appearance, very small chromosomes, such as the *IV*-chromosome of Drosophila (Fig. 166), and may, so far as we can tell, be composed entirely of chromatin.

Because of their ubiquity and the difficulty of excluding them from materials suitable for their growth, it was long supposed that bacteria might originate spontaneously from non-living matter. It has, however, been quite conclusively demonstrated, by many careful experiments, that no microscopically visible bacteria or putrefactive organisms of any kind appear in dead organic matter unless they gain access to it from outside. These experiments have been widely, but uncritically, cited as proving that living things are never "spontaneously generated" from non-living matter; all that they actually prove, of course, is that these particular kinds of organisms do not so originate under these particular conditions. It may, however, be safely assumed, on the basis of all our experience, that the ordinary, microscopically visible, bacteria originate only in the same way that higher organisms do—from previously living organisms of the same, or nearly the same, kind. These bacteria, simple as they appear to be in comparison with other unicellular organisms, are probably already much more complex than the simplest and earliest forms of life.

That living organisms might exist of such minute size as to be entirely invisible, even with the highest powers of the microscope, has long been suspected; and within the last thirty years the existence of many such organisms has been quite conclusively demonstrated. These are the filterable viruses (pp. 28, 143), parasitic ultramicrobes which infect bacteria, higher plants, and animals. The existence of these parasites is demonstrated by their pathogenic effects; at the present time at least fifty diseases are definitely known to be caused by infective agents of this type. There has been much discussion as to whether these viruses are really "alive," but this question turns entirely on the definition of "life." They certainly reproduce, or multiply, for if we inoculate a small quantity of one of these viruses into a healthy animal, this animal develops the characteristic disease after a certain length of time, and we find that a very small amount of its blood, when injected into another healthy animal, will infect this one, and so on for successive inoculations without limit; the virus must, therefore, multiply in each successive host, otherwise it would be lost by dilution after, at most, a few such transfers. This multiplication, moreover, is quite specific, for the same kind of host organism—even unicellular organisms, such as bacteria—may be infected with more than one kind of virus, each of which maintains its own specific characteristics while multiplying in the same kind of cells under the same conditions. These filterable viruses, therefore, have at least one of the most characteristic properties of living things—that of specific self-multiplication, or reproduction. This property necessarily implies some kind of metabolism, for, if the amount of virus increases, some material from its surroundings must be assimilated, or converted into the specific components of the virus. Metabolic processes of some kind may also be inferred from the pathogenic effects of the virus, indicating that it produces some kind of chemical change in its surroundings. Filterable viruses seem to possess, also, the property of mutability, as shown by the fact that some of the characteristics of a given strain can be altered by continued selection, and these altered characteristics persist in the selected race, indicating that they represent heritable variations. There is logical justification for regarding the properties of specific self-multiplication (specific autocatalysis) and mutability (heritable variation) as *the* essential characteristics of life, for, as we shall see later (p. 662), given these two properties all the other phenomena of life will eventually follow. There is also some indication that filterable viruses are composed, in part at least, of proteins, the most characteristic components of living things; for they give rise to phenomena of immunity, which, so far as all evidence shows, are elicited only by proteins (p. 634). In short, filterable viruses display some, at least, of the most distinctive general characteristics of living things; they must, therefore, logically be regarded either as living things or as intermediate between non-living and living things.

The size of the individual particles (or "cells") of filterable viruses can be determined, with a fair degree of accuracy, by their ability to pass through various grades of ultrafilters (*i.e.*, filters with ultramicroscopic pores) in comparison with colloidal particles of known size. The probable sizes of the virus particles, thus determined, range from 20 to 60 mμ ($2\text{–}6 \times 10^{-6}$ cm.) for different viruses. This is within the range of colloidal or ultramicroscopic dimensions (p. 62), and much smaller than the smallest microscopically visible bacteria (Fig. 4, *F*, *G*). It is, on the other hand, much larger than the probable size of the largest known protein molecules (Fig. 4, *H*). This leaves several possibilities as to the composition of the individual virus particle: it may be composed of several or many molecules, of the same or different kinds, with perhaps some kind of supramolecular structure comparable to, though simpler than, that of other organisms; it may be a single molecule much larger than any whose size has yet been determined by ordinary chemical methods; or it may consist of a single essentially living molecule, or gene, surrounded by a more extensive envelope of accessory material, comparable to cytoplasm, cell membranes, etc. If the virus particle be essentially a single molecule, then it represents the simplest conceivable type of living thing, a living molecule; *i.e.*, the virus is a living chemical substance.

It is obvious that the filterable viruses, as we know them, can not represent the first form of life to appear on the earth, for they are all parasitic, directly dependent on other organisms for their nutrition; indeed, no filterable virus has yet been found to multiply except within another living organism, though they may be kept alive, without increase, for long periods in non-living media. The first living things must necessarily be autotrophic, capable of assimilation of non-living materials from their environment. The question thus arises: are any non-parasitic ultramicroscopic organisms known? Some indication of the existence of such organisms in certain sulphurous springs has been adduced; but the evidence is still incomplete. The difficulty of this problem lies in demonstrating the existence of such organisms; for their existence could, presumably, be detected only by their chemical effects on their environment, and as we have no idea what their metabolic processes might be we do not know, *a priori*, what kind of chemical effects to look for. The conclusive demonstration of the existence of autotrophic, or even saprophytic, ultramicrobes would be an important step toward the solution of the problem of the origin of life. The next step, of course, would be to demonstrate that such simple living things can originate from non-living matter. The known filterable viruses originate, so far as we know, only in the same way that other organisms do—from previously living organisms of the same, or nearly the same, kind. Some students of the subject have believed that some of these viruses might originate "spontaneously" in the host organism, but there is no actual evidence of this; even if this were proved, it would not demonstrate their origin from non-living matter, for they might have been derived from living matter of the host—from a gene, perhaps, which had somehow "gone wrong." What is required is the demonstration of the origin of a living organism or substance in a medium which had previously contained no living matter—obviously a difficult thing to prove, for, in addition to the proof of the existence of such ultramicroscopic living things (the difficulties of which have been mentioned above), it would be necessary to prove that no living matter had been previously present in the medium, which might be still more difficult.

It has often been argued that, while living things must have originated from non-living matter at some time in the remote past, the conditions under which this happened may have been very different from those obtaining anywhere on the earth today, so that this "spontaneous generation" of life is no longer possible. In answer to this purely hypothetical argument, it may be said that conditions radically different from all those which exist anywhere on the earth at present—*e.g.*, conditions of temperature or pressure under which water could not exist in the liquid state—would probably be incompatible with any form of life. It has also been argued that, even if living things should originate from non-living matter at present, they could not survive in competition with those organisms which have become adapted to their environment by the long-continued action of natural selection. In view of the fact that long-established species are often displaced by new ones, introduced from other regions or originating by evolutionary changes, this argument is not very convincing; in any case, it has no bearing on the question of the possible *origin* of living things from non-living matter at present. In short, there seems to be no adequate reason to assume that living things, of the simplest kind, may not originate from non-living matter on the earth at the present time—but, on the other hand, there is not yet a scrap of evidence that they do.

The gene as the basis of life.—We have learned that the hereditary properties of organisms—*i.e.*, those properties inherent in the organism itself, as distinguished from those impressed upon it by its environment—are determined by genes: bodies or substances capable, in a suitable environment, of specific self-multiplication (specific autocatalysis) and also capable of heritable variation (mutation), *i.e.*, of changing in some way and yet retaining the property of specific self-multiplication in their new forms. Such bodies are present in the chromosomes of all organisms and also, to some extent, in the chloroplasts of plants. In the most primitive chlorophyl-bearing organisms, the Cyanophyceae (Fig. 10), the chromatin and the chlorophyl are not separated from each other by a nuclear membrane, as they are in higher plants; hence the nuclear genes and the chloroplast genes may well have had a common origin and only later, in the course of evolution, become separated. There is no evidence that genes exist anywhere else in the cell or the organism. There is, moreover, no evidence that any other components of the cell or the organism have the capacity of self-multiplication: the growth and reproduction of the cell and the organism are, so far as all evidence shows, results of the activities of the genes. Since growth and reproduction are certainly among the most distinctive characteristics of life, genes of some kind are absolutely essential to anything which we should recognize as "living."

But if the cell can not grow and reproduce without the genes, it is equally true, in all the ordinary "cellular" (unicellular or multicellular) organisms, that the genes can not grow and reproduce without the cell. The question therefore arises: do there exist any genes which are capable of exercising their peculiar property of specific autocatalysis apart from the complex structure of a cell? We immediately think of the filterable viruses, which have exactly the distinctive properties of genes: specific self-reproduction, mutability, and metabolic effects on their surroundings. The sizes of the filterable virus particles, so far as they have been determined (p. 658), also coincide very closely with the calculated size of the genes (p. 514). It must be remembered, of course, that all our present methods of calculating gene size give us merely the maximum size, not necessarily the most probable size, so that the genes may possibly be considerably smaller than the virus particles; but it is equally possible that there are viruses, or other ultramicroscopic organisms, smaller than those whose size has yet been determined. There are also some indications—though by no means conclusive evidence—that both the genes and the filterable viruses consist of, or contain, proteins (pp. 513, 658). On the whole, then, the individual particles of the filterable viruses seem to be rather closely comparable to the genes contained in the chromosomes of higher organisms. None of these viruses, however, have yet been shown to be capable of multiplying except within the cells of other organisms, so that it may still be contended that some of the non-genic components, and perhaps the structure, of the cell are necessary for the growth and reproduction of these as of other genes. What we still await is conclusive evidence of the existence of ultramicrobes capable of multiplying independently of other living organisms—true "free genes."

We have emphasized the properties of *specific autocatalysis* and *mutability* as the distinctive properties of the genes, and also (p. 658) as the most essential characteristics of life. By autocatalysis, in general, is meant the catalysis of a chemical reaction by one of its own products; *i.e.*, this product—the autocatalytic substance—brings about or accelerates the production of more of itself. There are many examples of autocatalysis, in this general sense, in non-living chemical systems; *i.e.*, reactions which are accelerated by some of their own products. But cases of highly specific autocatalysis, such as characterizes the gene—that is, the ability to bring about just that particular reaction which results in the formation of a product identical with itself, which will not otherwise occur at any appreciable rate and apparently can not be catalyzed by any other substance—are very unusual outside of living matter. But the gene has a still more peculiar property: it can mutate, *i.e.*, change in such a way that it now catalyzes specifically not the same reaction as before but a different one resulting in a product identical with its own new form. No such substance is known outside of living things—for the simple reason that any substance with these properties is, by virtue of these properties, *alive*. For, as we have seen (Chapter XXV), given the properties of multiplication and heritable variation, with the inevitable limitation of increase in a finite world, natural selection necessarily follows, resulting eventually in a multitude of diverse forms adapted to diverse environmental conditions. Any specifically autocatalytic and mutable substance must thus inevitably, if it persists at all, go through a process of evolution such as we believe living things to have actually undergone, resulting in some such diversified group of products as the organisms which now inhabit the earth. These considerations lead us to regard the gene as the essential basis of life: a gene, or "gene substance"—*i.e.*, a mutable, specifically autocatalytic substance—contains the potentiality of all the forms and phenomena of life.

On this view, the problem of the origin of life becomes the problem of the origin of genes. As we have previously seen (p. 512), very little is yet known of the composition and structure of genes: we may surmise, but can not yet prove, that they are proteins; we know that they are not greater than a certain ultramicroscopic size, but do not know how much smaller they may be; the facts of mutation (p. 572) strongly indicate that each gene is essentially a single molecule, though possibly (but not necessarily) larger and more complex than any molecules whose size and structure have yet been determined by chemical methods. To what peculiar features of composition or structure the genes owe their distinctive properties of specific autocatalysis and mutability, we have not yet the slightest idea. As to how, from what, and under what conditions, material with these peculiar properties may have originated, we can not, in the present state of knowledge, even guess. We know, however, that gene substance is being continually produced from non-genic materials, in living cells, by the autocatalytic action of the genes already present. But any reaction which occurs under the influence of a catalyst can, in theory at least, occur at some, perhaps inappreciable, rate in the absence of the catalyst; that is, any reaction which can be catalyzed is chemically *possible* without the catalyst, though its uncatalyzed rate may be practically infinitesimal—*i.e.*, no detectable amount of the product may be produced in any practically realizable period of time. In the case of the production of an autocatalytic substance, the slowness, however extreme, of the original uncatalyzed reaction is of no consequence once a single molecule of the substance has been produced, for it will then autocatalyze its own further production. There is, therefore, no theoretical difficulty, from the physicochemical standpoint, in the origin of living matter—*i.e.*, gene substance—from non-living substances. But the immediate precursors of the gene substance, in the cell, are presumably themselves complex organic compounds, resulting from a series of metabolic processes catalyzed by enzymes produced, directly or indirectly, by the action of the genes (p. 536); and we have no evidence of the existence of such complex organic compounds in nature apart from living organisms and their products. We thus seem to be faced by the dilemma that we can not get living matter (genes) except from complex organic compounds, and we can not get complex organic compounds (*i.e.*, "naturally") except from living matter. Many very complex organic substances, however, have been synthesized "artificially" by ordinary chemical methods, showing that the presence of living matter is not essential to their production; no compounds as complex as the natural proteins, it is true, have yet been produced "artificially," but there is not the slightest reason to assume that they can not be so produced by further extensions of our present methods (p. 54). Any molecule, however complex, whose formation is chemically possible, might, sooner or later, be formed from its constituent elements by pure chance (*e.g.*, as the end result of a series of chance molecular collisions and combinations), given sufficient time and material. Whether the amounts of these constituents in the earth and the length of time during which the earth has existed in a condition compatible with life are sufficient to render such chance formation of a gene molecule at all probable can not be even theoretically calculated until we know something of the actual composition and structure of the genes; at present we do not even know definitely, however probable it may seem, that the genes actually are composed of complex organic substances.

Whatever may be the probability of the non-autocatalyzed origin of a gene from lifeless matter, it must obviously be enormously greater than that of the "spontaneous generation" of a man, an amoeba, or even an ordinary bacterium. The most probable hypothesis, therefore, in the light of our present knowledge, seems to be that the simplest and earliest form of life was a single gene—that is, a specifically autocatalytic and mutable molecule. Given a substance with these properties, the evolution of all the higher forms of life seems quite explicable, in principle, by the operation of natural selection (Chapter XXV). It should be noted that there is nothing in this principle, or in the properties of the genes, to give any general "trend" of evolution toward greater complexity—or toward anything else, except greater fitness to survive and multiply. We find, in fact, in many groups of organisms, marked simplification of structure in the course of evolution. But if the earliest forms of life were the simplest possible ones, as we assume, the *average* course of evolution—that is, of diversification—must necessarily be in the direction of greater complexity; just as, if we put a crystal of some soluble substance in the bottom of a beaker of water, the *average* movement of the substance, by diffusion, will be upward, not because its molecules have any tendency to move upward rather than in any other direction, but because they all started at the bottom. Relatively simple types of organisms, such as bacteria, still comprise, in fact, by far the greatest number of individual living things, and probably the greatest bulk of living matter, on the earth today.

The principal stages of increasing structural complexity of living things may be summarized briefly as follows:

Evolutionary stages	*Existing representatives*
1. Genes	Filterable viruses (?)
2. Aggregates of genes	Smallest microscopic bacteria (?)
3. Elaboration of accessory materials: cytoplasm, chlorophyl, cell walls, etc.	Schizophytes
4. Development of mitotic mechanism	
5. Differentiation among genes	
6. Separation of nucleus and cytoplasm by nuclear membrane	Unicellular thallophytes and protozoa
7. Aggregates of cells	Colonial organisms
8. Differentiation among cells	Multicellular organisms

These stages need not necessarily all have occurred in exactly the order indicated. Stage *3* might probably precede *2* in many cases, for a single gene might well be surrounded by a "cytoplasmic" envelope of its metabolic by-products (p. 658). We know that stage *7* has preceded *6* (and perhaps also *4* and *5*) in many cases, for there are many colonial schizophytes. Stage *4* must, however, precede *5*, for a group of differentiated genes could not remain together through successive cell-generations without some kind of mechanism for their regular distribution to the daughter cells; and *4* must presumably be preceded by *3* to some extent. Stage *6* might conceivably precede *4* and *5*, but so far as we know every type of unicellular organism with distinct nucleus and cytoplasm has, in fact, some kind of mitotic mechanism (p. 359); whether, or to what extent, their genes are differentiated, we do not actually know; given an effective mitotic mechanism, however, differentiation among the genes must necessarily follow, for they would eventually become different by mutations.

All these advances in complexity of structure have come about, in the course of ages, by the action of natural selection. Those genes which happened to mutate in such a way as to produce, as by-products of their autocatalytic metabolism, substances or structures favorable to their further reproduction, survived and multiplied. From this viewpoint, the main lines of evolutionary advance have been: the production of a constant and favorable environment for the multiplication of the genes—first the cytoplasm, later (in multicellular organisms) the extracellular body-fluids; the development of mechanisms for the preservation and regulation of this internal environment; the development of more efficient methods of nutrition; and the development of various mechanisms for reproduction and dispersal and for protection or escape from enemies.

The first living things presumably obtained their nutrition—*i.e.*, the matter and energy necessary for their autocatalytic multiplication—from substances which happened to be present in their non-living environment, as the autotrophic bacteria still do (p. 144). One of the greatest, and presumably one of the earliest, advances in methods of nutrition was the production of chlorophyl (or some similar substance), enabling the organism to utilize the radiant energy of the sun, resulting eventually in the varied types of green plants, the primary feeders of the living world today. With the great increase of organic matter resulting from this development, other organisms adopted the saprophytic and parasitic methods of nutrition. The development of complex cytoplasmic structures made possible the holozoic method of nutrition, giving rise to the animal kingdom.

It will be noted, in our tabulation of evolutionary stages,

(p. 665), that the typical unicellular organisms, with distinct nucleus and cytoplasm, represent a relatively advanced stage—more than half way, so to speak, from the simplest to the most complex. This is confirmed by the evidence of fossil remains, so far as this evidence goes. For ages longer, probably, than the duration of all subsequent time, the only living things on the earth were organisms of the grade of bacteria and blue-green algae (Fig. 194). Such an organism as Amoeba, often spoken of as "one of the simplest living things," probably really represents a stage of evolution more than half way from the first gene to man.

On the view presented here—the view that seems in best accord with all our present knowledge—all the component substances and structures of cells and organisms, all the complex and varied phenomena of life, are essentially byproducts of the autocatalytic reproduction of the genes: they have been developed and preserved, by the action of natural selection, because they favor the multiplication of the genes which produce them. The nature and the operation of these various accessory components and activities of organisms present a host of still unsolved problems: problems whose solution will probably require a great extension of our present knowledge of physics and chemistry. But the central problem of biology—the essential "secret of life"—lies in the genes themselves: their composition and structure, how they are autocatalytically synthesized, and how they may have first originated from lifeless matter.

APPENDIX I

CLASSIFICATION OF ORGANISMS

THE principles of classification are discussed in the text (Chapters II and XXVI). The classification of organisms down to classes (in some cases to subclasses) is given in the following pages. The phyla, within each kingdom, and the classes within each phylum are arranged, so far as possible, in order of increasing complexity. The probable relations between the various phyla are discussed in the text (Chapter XXVI) and represented in Fig. 196.

The number of species given for each phylum is the approximate number of living species described and named. In many, probably most, phyla there are undoubtedly many more species still undescribed.

Kingdom **PLANTAE**:

Organisms usually having rigid cell walls; nutrition autotrophic, saprophytic, parasitic, or mixotrophic (p. 144). The line between the plant and animal kingdoms is not at all sharp, as explained in the text (pp. 30, 36).

Phylum **SCHIZOPHYTA**: unicellular or simple colonial organisms, with no sharp distinction between nucleus and cytoplasm and no sexual reproduction. (3,000 species.)

Class **Bacteria** (or **Schizomycetes**): the bacteria (pp. 29, 141; Figs. 10, 37, 39–41).

Class **Cyanophyceae** (or **Schizophyceae**): the blue-green algae (p. 30; Figs. 10, 112).

Phylum **THALLOPHYTA**: unicellular, colonial, or simple multicellular plants, with distinct nucleus and cytoplasm and usually some form of sexual reproduction; without true leaves, stems, or roots; usually without regular alternation of generations; ordinary cells usually haploid. (80,000 species.)

Class **Flagellata**: the flagellates (p. 140); these organisms, connecting the plant and animal kingdoms (Fig. 196), may be classified equally well as either Thallophyta or Protozoa. Example: *Euglena* (Fig. 36).

Class **Chlorophyceae**: the green algae; a rather heterogenous group, often divided into several classes. Examples: *Pleurococcus* (Fig. 12), *Chlamydomonas* (Fig. 30), *Volvox*, etc. (Figs. 118, 121), *Closterium* (Fig. 30), *Spirogyra* (Figs. 14, 119, 122), diatoms (p. 377), *Vaucheria* (Fig. 13), *Ulothrix* (Figs. 42, 117, 120), *Oedogonium* (Fig. 140), *Nitella* (Fig. 43).

Class **Phycomycetes**: simple fungi (molds) with syncytial mycelia. Example: *Mucor* (Fig. 35).

Class **Phaeophyceae**: the brown algae (pp. 123, 160, 376, 426).

Class **Rhodophyceae**: the red algae (pp. 123, 376, 426).

Class **Eumycetes**: fungi with multicellular mycelia (except in the unicellular yeasts); often divided into two classes, Ascomycetes and Basidiomycetes. Examples: yeasts (Figs. 34, 115, 116), *Aspergillus* (Fig. 35), mushrooms, puffballs, etc. (p. 136).

Phylum **BRYOPHYTA**: multicellular, usually terrestrial, plants, with regular alternation of generations; the sporophyte always dependent on the gametophyte. (17,000 species.)

Class **Hepaticae**: the liverworts; usually simple, flat plants without stem or leaves.

Class **Musci**: the mosses (Figs. 44, 141).

Phylum **PTERIDOPHYTA**: vascular plants with regular alternation of generations; both generations usually independent, but the sporophyte much the larger and longer-lived. (5,000 species.)

Class **Filicineae**: the ferns (Figs. 46, 142).

Class **Equisetineae**: the horsetails or scouring-rushes.

Class **Lycopodineae**: the club-mosses. Example: *Selaginella* (Fig. 143).

Phylum **SPERMATOPHYTA**: the seed-plants, vascular plants reproducing by seeds; gametophyte very small and dependent on the sporophyte. (130,000 species.)

Subphylum **GYMNOSPERMAE**: conifers, cycads, etc.; no ovary or true flowers (p. 434).

Subphylum **ANGIOSPERMAE**: flowering plants; ovules completely enclosed in an ovary (Figs. 144–146).

Class **Monocotyledoneae**: grasses, lilies, orchids, etc.; embryo with a single cotyledon; vascular bundles scattered through the stem; leaves with parallel veins; flower parts in threes or sixes (Fig. 46).

Class **Dicotyledoneae**: most flowering plants; embryo with two cotyledons; vascular bundles in a ring in the stem; leaves with net-like venation; flower parts in fours or fives (Figs. 46, 47, 145, 147–149).

Kingdom **ANIMALIA**:

Organisms usually without rigid cell walls or chlorophyl; nutrition usually holozoic (p. 145).

Phylum **PROTOZOA**: unicellular or simple colonial animals, usually with distinct nucleus and cytoplasm; with or without sexual reproduction. (8,000 species.)

Class **Flagellata** (or **Mastigophora**): the flagellates (see p. 669).

Class **Rhizopoda** (or **Sarcodina**): protozoa with pseudopodia. Examples: *Amoeba* (Figs. 11, 26, 114), slime molds (Fig. 13). (The slime molds are sometimes classified as plants, because their spores have cellulose cell walls.)

Class **Sporozoa**: parasitic protozoa, usually without locomotive or ingestive organs.

Class **Infusoria**: protozoa with cilia. Examples: *Paramecium* (Fig. 27), *Vorticella* (Fig. 75).

All the following phyla, consisting of multicellular animals, are called collectively Metazoa; the groups Protozoa and Metazoa are sometimes called subkingdoms.

Phylum **PORIFERA**: the sponges, simple multicellular animals with little "individuality," forming branching, non-motile colonies. (2,000 species.)

Phylum **COELENTERATA**: radially symmetrical, diplobastic ("two-layered") animals. (4,000 species.)

Class **Hydrozoa**: hydra-like animals, often colonial, and often having a regular alternation of asexual and sexual generations. Example: *Hydra* (Figs. 54, 77, 124, 138).

Class **Scyphozoa**: jellyfishes.

Class **Anthozoa** (or **Actinozoa**): sea-anemones and corals.

Class **Ctenophora**: jellyfish-like animals, somewhat more complex in structure than the typical coelenterates, and often classified as a separate phylum.

Phylum **PLATYHELMINTHES**: the flatworms, bilaterally symmetrical, triploblastic ("three-layered") animals, without a true body cavity or an anus. (5,000 species.)

Class **Turbellaria**: non-parasitic flatworms. Example: *Planaria* (Figs. 55, 56).

Class **Trematoda**: the flukes, parasitic flatworms with an enteron.

Class **Cestoda**: the tapeworms, parasitic flatworms with no enteron, absorbing nourishment through the body surface.

The two following classes are somewhat more complex in structure than the typical flatworms, and are often classified as separate phyla. Their closest relationships are probably to the flatworms, and they may be included in this phylum as a matter of convenience.

Class **Nemertinea**: worms resembling flatworms, but with an anus and blood-vessels.

Class **Rotifera**: microscopic, usually free-swimming, animals, with an anus and body-cavity (p. 418).

Phylum **NEMATHELMINTHES**: the roundworms, elongate cylindrical worms with an anus and body-cavity. The relationship of the three classes included here is doubtful; they are placed together in this phylum as a matter of convenience. (1,500 species.)

Class **Nematoda**: the typical roundworms, including both free-living and parasitic forms.

Class **Acanthocephala**: parasitic worms with no enteron, absorbing nourishment through the body surface.

Class **Chaetognatha**: free-swimming, marine worms, of somewhat more complex structure than the typical roundworms; coelom developed from enteric pouches, as in the two following phyla and the lower chordates.

Phylum **PROSOPYGIA** (or **MOLLUSCOIDA**): animals with a true coelom, developed from enteric pouches; the enteron U-shaped, so that the anus is near the mouth. (2,000 species.)

Class **Bryozoa** (or **Polyzoa**): minute animals forming branching colonies, superficially resembling colonial hydroids.

Class **Phoronida**: worm-like animals living in membranous tubes in the sand.

Class **Brachiopoda**: animals forming shells resembling those of bivalve molluscs.

Phylum **ECHINODERMATA**: radially symmetrical animals, with well-developed coelom formed from enteric pouches. (3,000 species.)

Class **Crinoidea**: feather-stars, sessile animals often having a jointed stalk for attachment.

Class **Asteroidea**: starfishes (Fig. 130).

Class **Ophiuroidea**: brittle-stars.

Class **Echinoidea**: sea-urchins.

Class **Holothuroidea**: sea-cucumbers.

Phylum **ANNELIDA** (or **ANNULATA**): segmented worms, usually with well-developed coelom and blood-vessels. (4,000 species.)

Class **Archiannelida**: marine worms, simpler than other annelids.

Class **Chaetopoda**: marine, fresh-water, and terrestrial segmented worms. Example: earthworm (Figs. 58–61, 79, 132).

Class **Hirudinea**: leeches.

Class **Gephyrea**: marine worms of doubtful relationships, unsegmented in the adult stage.

Phylum **MOLLUSCA**: unsegmented animals, usually with a shell. (60,000 species.)

Class **Amphineura**: the simplest types of molluscs; *Chiton*, etc.

Class **Pelecypoda**: bivalve molluscs; clams, oysters, mussels, scallops, etc.

Class **Scaphopoda**: molluscs with a conical tubular shell; *Dentalium*, etc.

Class **Gastropoda**: asymmetrical molluscs, usually with a spiral shell; snails, etc.

Class **Cephalopoda**: octopus, squid, cuttlefish, nautilus, etc.

Phylum **ARTHROPODA**: segmented animals with jointed appendages. (400,000 species.)

Class **Crustacea**: lobsters, crabs, crayfishes, shrimps, etc.

Class **Arachnida**: spiders, mites, scorpions, etc.

Class **Onychophora**: simple, worm-like, terrestrial arthropods; *Peripatus*.

Class **Myriapoda**: centipedes and millipedes.

Class **Insecta**: insects. Example: *Drosophila* (Figs. 159, etc).

Phylum **CHORDATA**: animals having at some stage a notochord, gill-slits, and a hollow nerve-cord on the dorsal side. (30,000 species.)

Subphylum HEMICHORDA (or ENTEROPNEUSTA): worm-like animals with a notochord-like structure in the head end; *Balanoglossus*, etc. (p. 650).

Subphylum **UROCHORDA** (or **TUNICATA**): tunicates; sac-like, usually sessile animals, often forming branching colonies; in the larval stage they have a notochord in the tail region (p. 650).

Subphylum **CEPHALOCHORDA**: lancelets; somewhat fish-like animals, with a permanent notochord the whole length of the body; no cartilage or bone (p. 649).

Subphylum **VERTEBRATA**: the vertebrates; notochord surrounded or replaced by cartilage or bone, forming the vertebral column or backbone (p. 195; Fig. 62).

Class **Cyclostomata**: lampreys and hagfishes, eel-like animals without limbs or jaws.

Class **Pisces**: fishes, aquatic vertebrates breathing by gills; single circulation; skin usually covered with scales; the limbs are fins (Figs. 68, 70, 193).

Subclass *Elasmobranchii*: cartilaginous fishes, with no air-bladder or lung; sharks and skates.

Subclass *Teleostomi*: bony fishes, usually having an air-bladder or lung; including the Crossopterygii, Dipnoi (lungfishes), ganoids, and teleosts (Fig. 197); the first three of these groups are almost extinct, the teleosts comprising the great majority of living fishes.

Class **Amphibia**: salamanders, frogs, and toads; usually breathing by gills in the larval stage, by lungs in the adult stage; incomplete double circulation; skin usually naked; the limbs are legs; no embryonic membranes (Figs. 63, 68, 102, 125, 133, 178, 179, 192).

Class **Reptilia**: turtles, lizards, snakes, crocodiles; breathing by lungs; incomplete double circulation; skin usually covered with scales; the limbs are legs (absent in snakes); embryo with amnion and allantois (Fig. 192).

Class **Aves**: the birds, warm-blooded animals with complete double circulation, skin covered with feathers, the fore-limbs wings; embryo with amnion and allantois (Figs. 192, 193).

Class **Mammalia**: the mammals, warm-blooded animals with complete double circulation, skin usually covered with hair, young nourished with milk secreted by the mother; embryo with amnion and allantois; limbs usually legs (fore-limbs sometimes arms, wings, or fins).

Subclass *Prototheria* (or *Monotremata*): the monotremes, oviparous mammals with imperfect temperature regulation; only two living species, the duck-bill and spiny anteater of Australia (pp. 402, 646).

Subclass *Metatheria* (or *Marsupialia*): the marsupials, viviparous mammals without a placenta (or with a poorly developed one), the young carried in an external pouch of the mother for some time after birth; kangaroos, opossums, etc. (pp. 406, 646).

Subclass *Eutheria*: mammals with a well-developed placenta

(Fig. 134), comprising the great majority of living mammals. The principal orders of Eutheria (Fig. 197) are the following:

Insectivora: shrews, moles, hedgehogs, etc.

Edentata: toothless mammals; anteaters, sloths, armadillos, etc.

Rodentia: the rodents; rabbits, rats, mice, squirrels, etc.

Ungulata: hoofed animals; cattle, deer, camels, swine, horses, elephants, etc. (often divided into several orders).

Sirenia: the manatee and dugong, aquatic mammals with the fore-limbs fin-like, the hind limbs absent.

Carnivora: carnivorous animals; cats, dogs, bears, weasels, seals, etc. (Fig. 192).

Cetacea: the whales, dolphins, and porpoises, aquatic mammals with the fore-limbs fins, the hind limbs absent (Fig. 192).

Chiroptera: the bats, aerial mammals with the fore-limbs wings (Fig. 192).

Primates: the lemurs, monkeys, apes, and man (Figs. 65, 103, 126, 134, 192, 193, 198).

APPENDIX II

CHEMICAL SYMBOLISM AND NOMENCLATURE; CLASSIFICATION OF CHEMICAL COMPOUNDS

ALL the phenomena of life involve chemical processes. Every phase of biology therefore necessarily deals largely with chemical processes. The representation of chemical processes is greatly facilitated by the employment of the system of symbolism, or "chemical shorthand," which has been developed by chemists. The essential principles of this system, sufficient to understand all the chemical formulas and terms used in this book, are presented in the following pages.

Each kind of *atom* is represented by a *symbol*, consisting of either one or two letters (the first always capitalized). These symbols are often used to stand for the names of the elements, but more strictly the symbol represents *one atom* of the element; *e.g.*

O = an *oxygen atom*
Cl = a *chlorine atom*
Na = a *sodium atom*

The symbols of all the elements of biological importance are given on p. 39 (see also Fig. 2).

Each kind of *molecule*, of a free element or a compound, is represented by a *formula* which shows the *kinds of atoms* and the *number of each kind* in the molecule. These formulas are often used instead of the names of the substances they represent, but more strictly the formula represents *one molecule* of the substance; *e.g.*,

O_2 = a *molecule* of *free oxygen*, consisting of two oxygen atoms chemically combined (see Fig. 1).
H_2O = a *molecule* of *water*, consisting of two hydrogen atoms and one oxygen atom (see Figs. 1 and 3).
H_2O_2 = a *molecule* of *hydrogen peroxide*, consisting of two hydrogen and two oxygen atoms.

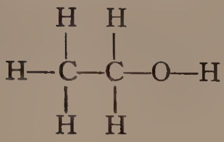
The order in which the symbols of the different atoms in a molecule are written is usually of no special significance, but in molecules which are made up of two or more *radicals*—groups of atoms which act as units in many chemical changes—this fact is usually indicated in the formula; *e.g.*,

CH_3OH = a molecule of *methyl alcohol*, made up of a *methyl* radical (CH_3) and a *hydroxyl* radical (OH).
$C_3H_5(OH)_3$ = a molecule of *glycerol*, made up of a *glyceryl* radical (C_3H_5) and three *hydroxyl* radicals.

Each kind of *ion* is represented by a formula which shows its atomic constituents (as in a molecular formula) and also the *number* and *kind* (positive or negative) of *electric charges* it carries. A *single negative charge* means an excess of one electron (*i.e.*, the ion has one more electron than protons); a *single positive charge* means a deficiency of one electron (one less electron than protons); *e. g.*,

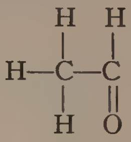
Na^+ = a *sodium ion*, consisting of a sodium atom which has lost one electron.
Ca^{++} = a *calcium ion*, consisting of a calcium atom which has lost two electrons.
Cl^- = a *chlorine ion*, consisting of a chlorine atom which has gained one extra electron.
NH_4^+ = an *ammonium ion*, consisting of one nitrogen and four hydrogen atoms, this radical *as a whole* having a deficiency of one electron
SO_4^{--} = a *sulphate ion*, consisting of one sulphur and four oxygen atoms, this radical *as a whole* having an excess of two electrons. (See also table on page 42.)

Formulas of the types shown above indicate only the *kinds* and *numbers* of atoms in the molecule (or ion); these are called *empirical formulas*. To indicate also the *relations* of the atoms within the molecule another kind of formula, called a *structural formula*, is used. Among inorganic substances there is usually only one compound having a particular empirical formula; structural formulas are therefore seldom used for these substances. Among organic substances, however, there are often several or many compounds having the same empirical formula; *i.e.*, their molecules contain the same kinds and same number of each kind of atoms, but differ in the *arrangement* of these atoms in the molecules. It is therefore necessary to employ structural formulas to indicate the differences between these compounds (see pp. 47, 113, etc.). It is impossible, of course, to show on paper the actual three-dimensional arrangement of the atoms; a structural formula does not attempt to do this, but merely to show which atoms are directly attached to each other and how they are attached; a single line connecting the symbols of two atoms indicates that these atoms are attached to each other by a single "chemical bond," which means a single *pair of electrons* shared by the two atoms (see Fig. 3); two lines indicate a "double bond," *i.e.*, two *pairs* of electrons shared by the two atoms; three lines a "triple bond" or three *pairs* of shared electrons. The structural formula of *ethyl alcohol*,



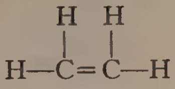
$$\begin{array}{ccccccccc} & & H & & H & & & & \\ & & \vert & & \vert & & & & \\ H & - & C & - & C & - & O & - & H \\ & & \vert & & \vert & & & & \\ & & H & & H & & & & \end{array}$$

indicates that in this molecule the two carbon atoms are united by a single bond (*i.e.*, they share one pair of electrons with each other), three of the hydrogen atoms are directly attached to one carbon and two to the other carbon in the same way, the oxygen atom is also attached to this second carbon atom by a single bond and to the remaining hydrogen atom by another single bond (compare Fig. 3). In *acetaldehyde*,



$$\begin{array}{ccccc} & & H & & H \\ & & \vert & & \vert \\ H & - & C & - & C \\ & & \vert & & \Vert \\ & & H & & O \end{array}$$

all the hydrogen atoms are attached directly to carbon atoms, and the oxygen atom is attached to a carbon atom by two bonds (*i.e.*, these two atoms share two pairs of electrons with each other). In some organic compounds, carbon atoms are attached to each other by double or triple bonds (*i.e.*, they share two or three pairs of electrons with each other); *e.g.*,



$$\begin{array}{ccccccc} & & H & & H & & \\ & & \vert & & \vert & & \\ H & - & C & = & C & - & H \end{array}$$

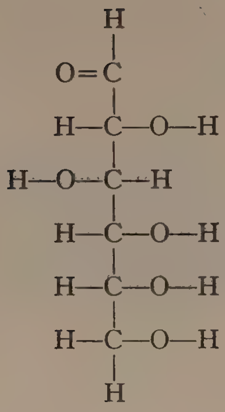
ethylene

$H{-}C{\equiv}C{-}H$

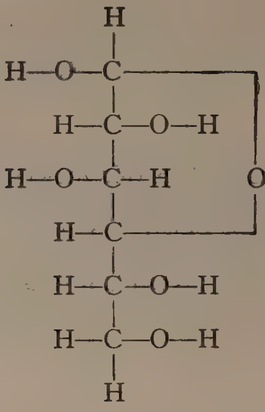
acetylene

(Double and triple bonds do not make the union between the atoms they connect "stronger"; on the contrary, such bonds are actually "weaker" than single bonds, in the sense that the molecules are more reactive chemically at these points.) The experimental evidence on which structural formulas are based is presented in textbooks of organic chemistry.

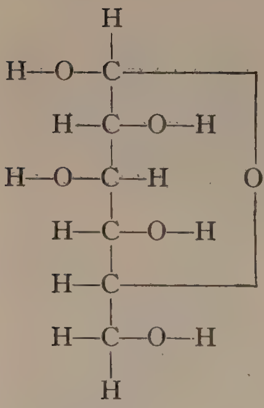
The student may be confused by finding different structural formulas for the same substance in different books, or even in the same book. Some of these differences are merely different ways of writing the same formula; others may represent different forms of molecules which are regarded (for reasons into which we need not go here) as different "varieties" of the same substance rather than as distinct substances; while some of these discrepancies represent changes in our ideas of the correct formula due to increasing knowledge. For instance, all the following, and a number of other, structural formulas will be found for *glucose* (also called *d-glucose* or *dextrose*):



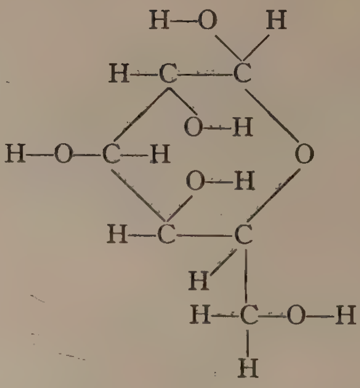
(1)



(2)



(3)



(4)

Of these four formulas, it will be seen on careful inspection that the third and fourth are merely different ways of writing the same thing, the third being the more customary way (the length and shape of the line connecting two symbols, *e.g.*, C and O, is of no significance, as the structural formula does not attempt to represent the actual spatial configuration of the atoms). The first and second formulas represent successive theories of the structure of the normal glucose molecule, but these forms of molecules are now believed to be present in only small proportions in ordinary glucose solutions, while the third (or fourth) formula represents the most common form of the normal glucose molecule, on the basis of the latest and best evidence.

Frequently, to save space, instead of the complete structural formula, types of formulas intermediate between the empirical and structural formulas are used; for instance *palmitic acid* may be represented by any one of the following formulas:

$C_{16}H_{32}O_2$
$H{\cdot}C_{16}H_{31}O_2$
$C_{15}H_{31}COOH$
$CH_3(CH_2)_{14}COOH$

or the complete structural formula (p. 49). The first of these is the empirical formula, showing only the number of *atoms* of each kind in the molecule; the second shows that the molecule contains one *ionizable* hydrogen atom; the third shows that it contains a *carboxyl radical* (COOH); the fourth shows all the kinds of *radicals*, and the number of each, in the molecule. In particular, very common radicals such as CH_3, CH_2, OH, NH_2, COOH, etc., are usually written in this way rather than in their complete structural forms.

Chemical reactions—changes of one or more substances into different substances, by recombination of their constituent atoms into different kinds of molecules—are represented by *chemical equations*. A chemical equation shows all the *kinds of molecules* involved in the reaction—as reacting substances or products—and the *relative numbers* of each kind involved; *e.g.*,

$$2\ H_2 + O_2 \longrightarrow 2\ H_2O$$

This equation indicates: "two molecules of free hydrogen and one molecule of free oxygen react to form two molecules of water." Since *atoms* are never changed (*i.e.*, into different kinds of atoms) in any chemical reaction, the number of atoms of each kind must always be *equal on both sides of the equation*. Thus, in the above equation, there are four hydrogen and two oxygen atoms on the left side (two hydrogen molecules each consisting of two atoms, and one oxygen molecule of two atoms) and likewise four hydrogen and two oxygen atoms on the right side (two water molecules each consisting of two hydrogen and one oxygen atoms). The number of each kind of molecules in the equation must always be such as to satisfy this condition. Any of the types of formulas described above may be used in chemical equations.

The equation written above represents the reaction *in one direction only*, as indicated by the arrow; *i.e.*, the combination of hydrogen and oxygen to form water, but not the reverse reaction (decomposition of water into hydrogen and oxygen). In fact, however, any chemical reaction may proceed *in either direction*, depending on certain conditions (see p. 96). When we wish to indicate that a reaction, *under the particular conditions we are discussing*, proceeds in one direction only (or practically so), we use a single arrow as above. When we wish to include in our discussion both of the two opposite reactions—*e.g.*, the formation and decomposition of water—we use double arrows, thus:

$$2\ H_2 + O_2 \rightleftharpoons 2H_2O$$

A chemical equation shows the *initial reactants* and the *final products* of a chemical change, without necessarily implying that this change occurs directly in a single reaction. For instance, the complete oxidation of glucose, under any conditions, may be represented by the equation

$$C_6H_{12}O_6 + 6\ O_2 \longrightarrow 6\ CO_2 + 6\ H_2O$$

which shows merely the substances used up (glucose and free oxygen) and the final products (carbon dioxide and water). This process, however, probably always involves a number of intermediate steps in the decomposition of the glucose molecule and the oxidation of its constituent atoms, the nature of these intermediate reactions depending on the particular conditions under which the process occurs. Some of the intermediate steps in the oxidation of glucose in the living cell are shown in Chapter VII (p. 113). Thus the same chemical process may be represented by a single equation, as above, or by a series of equations, as on p. 113, according to whether we are interested, at the moment, in the end result only or in the intermediate steps.

Chemical compounds are *classified* into *inorganic* and *organic* compounds. Organic compounds include all compounds containing *carbon*, except a few very simple ones such as CO, CO_2 and the carbonates (p. 42) which, together with all compounds not containing carbon, are classed as inorganic. The distinctive differences between these two classes of compounds are discussed on p. 44.

Inorganic compounds are classified according to the kinds of *ions* of which they are composed, or which they form when dissolved in water (p. 9). *Water* forms hydrogen and hydroxyl ions (H^+ and OH^-); *acids* form hydrogen but not hydroxyl ions; *bases* form hydroxyl but not hydrogen ions; *salts* form cations other than H^+ and anions other than OH^-. The composition and interrelations of these four classes of substances may be illustrated thus (A^- representing any anion except OH^-, and B^+ any cation except H^+):

$$\begin{array}{ccccc} & & \text{water} & & \text{salt} \\ & & \downarrow\uparrow & & \downarrow\uparrow \\ \text{acid} & \rightleftharpoons & H^+ & + & A^- \\ & & + & & + \\ \text{base} & \rightleftharpoons & OH^- & + & B^+ \end{array}$$

Any acid and any base, when mixed together, react to form water and a salt: this is called *neutralization.* The terms acid and base are generally applied not only to substances which form hydrogen or hydroxyl ions by simple dissociation, as indicated above, but also to substances like carbon dioxide (CO_2) and ammonia (NH_3) which form these ions by reacting with water, thus:

$$CO_2 + H_2O \rightleftharpoons H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$$

$$NH_3 + H_2O \rightleftharpoons NH_4OH \rightleftharpoons NH_4^+ + OH^-$$

Any solution containing more hydrogen than hydroxyl ions is *acidic*; one containing an excess of hydroxyl ions is *basic* (or *alkaline*); one containing equal numbers of these two kinds of ions is *neutral*.

Most salts, and a few acids and bases, are *strong electrolytes*, which are completely (or almost completely) ionized under all conditions. Many acids and bases are *weak electrolytes*, which are only partially ionized; *i.e.*, only a relatively small proportion of their molecules are dissociated into ions under most conditions. Water is a *very weak* electrolyte, ionizing only to the extent of about 1 molecule in 555,000,000. For this reason, no considerable amounts of both hydrogen and hydroxyl ions can ever be present simultaneously in the same solution, for all but a very small proportion of them always combine to form undissociated water (H_2O) molecules.

An acid containing more than one ionizable hydrogen atom may form different anions according to how many hydrogen ions it dissociates; *e.g.*,

$$CO_2 + H_2O \rightleftharpoons \underset{\substack{\text{carbonic}\\ \text{acid}}}{H_2CO_3} \rightleftharpoons H^+ + \underset{\substack{\text{bicarbonate}\\ \text{ion}}}{HCO_3^-} \rightleftharpoons 2\ H^+ + \underset{\substack{\text{normal}\\ \text{carbonate}\\ \text{ion}}}{CO_3^{--}}$$

$$\underset{\substack{\text{phosphoric}\\ \text{acid}}}{H_3PO_4} \rightleftharpoons H^+ + \underset{\substack{\text{primary}\\ \text{phosphate}\\ \text{ion}}}{H_2PO_4^-} \rightleftharpoons 2\ H^+ + \underset{\substack{\text{secondary}\\ \text{phosphate}\\ \text{ion}}}{HPO_4^{--}} \rightleftharpoons 3\ H^+ + \underset{\substack{\text{normal}\\ \text{phosphate}\\ \text{ion}}}{PO_4^{---}}$$

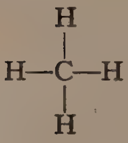
Each of these kinds of anions forms salts; *e.g.*,

$NaHCO_3$ sodium bicarbonate } both called
Na_2CO_3 normal sodium carbonate } "carbonates"
NaH_2PO_4 primary (monobasic) sodium phosphate
Na_2HPO_4 secondary (dibasic) " "
Na_3PO_4 normal (tribasic) " "

These examples illustrate the method of *naming* salts, by combining the names of the ions of which they are composed.

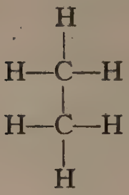
Organic compounds are classified according to the kinds of *radicals* which they contain and the ways in which these are joined together. Only a few of these classes, including those of most importance in biology, will be mentioned here.

Hydrocarbons are compounds containing only *carbon* and *hydrogen*. There are a great many different hydrocarbons, differing in the numbers of carbon and hydrogen atoms and the ways in which the carbon atoms are joined together—by single, double, or triple bonds, in straight or branched chains or closed rings—*e.g.*,



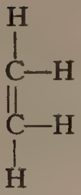
$$\begin{array}{c} H \\ | \\ H-C-H \\ | \\ H \end{array}$$

methane



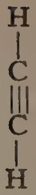
$$\begin{array}{c} H \\ | \\ H-C-H \\ | \\ H-C-H \\ | \\ H \end{array}$$

ethane



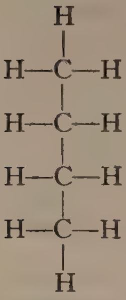
$$\begin{array}{l} H \\ | \\ C-H \\ \| \\ C-H \\ | \\ H \end{array}$$

ethylene



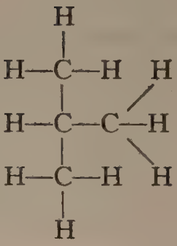
$$\begin{array}{c} H \\ | \\ C \\ ||| \\ C \\ | \\ H \end{array}$$

acetylene

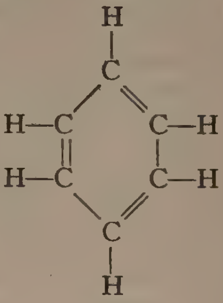


$$\begin{array}{c} H \\ | \\ H-C-H \\ | \\ H-C-H \\ | \\ H-C-H \\ | \\ H-C-H \\ | \\ H \end{array}$$

butane



isobutane

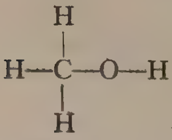


benzene

Hydrocarbons are of little direct importance in biology, but are of fundamental importance for understanding the chemistry of organic substances, since *all other organic compounds may be derived, theoretically, from hydrocarbons by substituting other atoms or radicals for one or more of the hydrogen atoms.* (They are not, however, actually produced in this way in the living cell.) Most of the examples used in the following paragraphs are derivatives of the simpler types of hydrocarbons, but many compounds of the same classes contain more complex carbon chains or rings, as shown in various illustrations in the text.

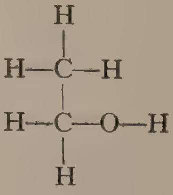
Oxygen compounds.—Almost all the organic compounds found in organisms contain *oxygen* in addition to carbon and hydrogen. Some of the simpler types containing *only* these three elements are the following:

Alcohols contain one or more *hydroxyl* (OH) radicals, but never more than one such radical attached to the same carbon atom; *e.g.*,



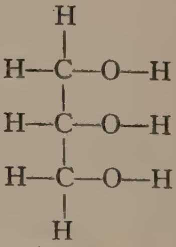
$$\begin{array}{l} \;\;H \\ \;\;\;| \\ H-C-O-H \\ \;\;\;| \\ \;\;H \end{array}$$

methyl
alcohol



$$\begin{array}{l} \;\;H \\ \;\;\;| \\ H-C-H \\ \;\;\;| \\ H-C-O-H \\ \;\;\;| \\ \;\;H \end{array}$$

ethyl
alcohol

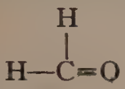


$$\begin{array}{l} \;\;H \\ \;\;\;| \\ H-C-O-H \\ \;\;\;| \\ H-C-O-H \\ \;\;\;| \\ H-C-O-H \\ \;\;\;| \\ \;\;H \end{array}$$

glycerol

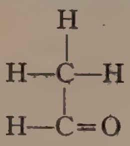
Alcohols are practically non-electrolytes. (Alcohols are *not* bases, although they contain hydroxyl *radicals*, because they do not form hydroxyl *ions*.)

Aldehydes contain the radical CHO (which can only occur at the *ends* of a carbon chain); *ketones* contain the radical CO, attached to two other carbon atoms; *e.g.*,



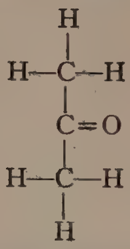
$$\begin{array}{ccc} & \mathrm{H} & \\ & | & \\ \mathrm{H}- & \mathrm{C} & =\mathrm{O} \end{array}$$

formaldehyde



$$\begin{array}{ccc} & \mathrm{H} & \\ & | & \\ \mathrm{H}- & \mathrm{C} & -\mathrm{H} \\ & | & \\ \mathrm{H}- & \mathrm{C} & =\mathrm{O} \end{array}$$

acetaldehyde

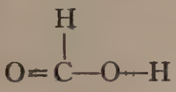


$$\begin{array}{ccc} & \mathrm{H} & \\ & | & \\ \mathrm{H}- & \mathrm{C} & -\mathrm{H} \\ & | & \\ & \mathrm{C} & =\mathrm{O} \\ & | & \\ \mathrm{H}- & \mathrm{C} & -\mathrm{H} \\ & | & \\ & \mathrm{H} & \end{array}$$

acetone
(di-methyl ketone,

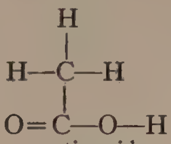
Aldehydes and ketones are non-electrolytes.

Organic acids contain one or more *carboxyl* (COOH) radicals; *e.g.*,



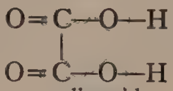
$$\begin{array}{ccc} & \mathrm{H} & \\ & | & \\ \mathrm{O}= & \mathrm{C} & -\mathrm{O}-\mathrm{H} \end{array}$$

formic acid



$$\begin{array}{ccc} & \mathrm{H} & \\ & | & \\ \mathrm{H}- & \mathrm{C} & -\mathrm{H} \\ & | & \\ \mathrm{O}= & \mathrm{C} & -\mathrm{O}-\mathrm{H} \end{array}$$

acetic acid

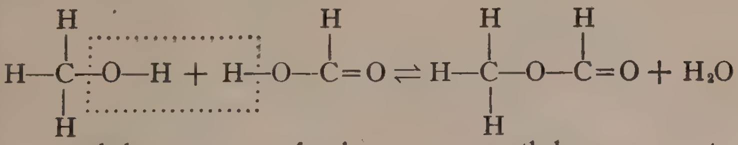


$$\begin{array}{ccc} \mathrm{O}= & \mathrm{C} & -\mathrm{O}-\mathrm{H} \\ & | & \\ \mathrm{O}= & \mathrm{C} & -\mathrm{O}-\mathrm{H} \end{array}$$

oxalic acid

(see also p. 49). The H of the carboxyl radical is *ionizable*, and any compound containing this radical therefore acts as an acid; most organic acids are, however, weak acids (*i.e.*, only a small proportion of their molecules are ionized under most conditions). Like inorganic acids, they form *salts* by reacting with bases; most of these salts are, like other salts, strong electrolytes (completely or almost completely ionized).

Esters are compounds formed of an alcohol minus its OH radicals and an acid (either organic or inorganic) minus its ionizable hydrogen atoms; *e.g.*,



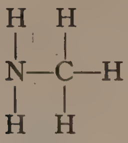
$$\begin{array}{cccccccccc} & \mathrm{H} & & & \mathrm{H} & & \mathrm{H} & & \mathrm{H} & \\ & | & & & | & & | & & | & \\ \mathrm{H}- & \mathrm{C} & -\mathrm{O}-\mathrm{H}+\mathrm{H}-\mathrm{O}- & & \mathrm{C} & =\mathrm{O}\rightleftharpoons\mathrm{H}- & \mathrm{C} & -\mathrm{O}- & \mathrm{C} & =\mathrm{O}+\mathrm{H_2O} \\ & | & & & & & | & & & \\ & \mathrm{H} & & & & & \mathrm{H} & & & \end{array}$$

methyl alcohol | formic acid | methyl formate | water

(see also p. 49). Esters are practically non-electrolytes.

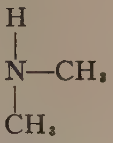
Nitrogen compounds.—Most of the nitrogenous organic compounds of biological importance contain radicals derived from ammonia (NH_3) or ammonium hydroxide (NH_4OH) by removal of one or more of their hydrogen atoms; *e.g.*, the *amino* radical (NH_2), the *imino* radical (NH), etc.

Most of these organic nitrogen compounds act as *bases*, like ammonia itself (p. 681), and are therefore called *organic bases.* The simplest organic bases are the *amines*; *e.g.*,



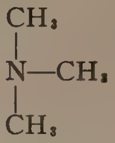
$$\begin{array}{ccccc} H & & H & & \\ | & & | & & \\ N & — & C & — & H \\ | & & | & & \\ H & & H & & \end{array}$$

methyl amine



$$\begin{array}{ccc} H & & \\ | & & \\ N & — & CH_3 \\ | & & \\ CH_3 & & \end{array}$$

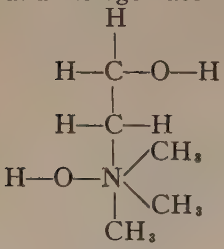
di-methyl amine



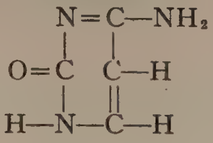
$$\begin{array}{ccc} CH_3 & & \\ | & & \\ N & — & CH_3 \\ | & & \\ CH_3 & & \end{array}$$

tri-methyl amine

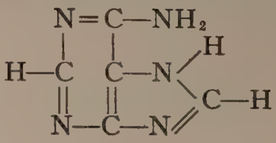
Most of the organic bases found in organisms, however, are more complex substances, many of them containing "rings" of carbon and nitrogen atoms; *e.g.*,



choline



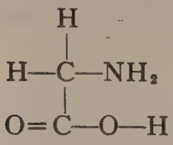
cytosine



adenine

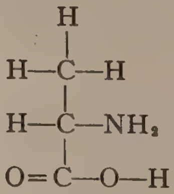
These organic bases usually occur, in organisms, as constituent radicals of still more complex molecules; *e.g.*, choline in lecithins (p. 50); cytosine, adenine, and other similar bases in nucleic acids (p. 513).

Amino-acids are compounds containing both the *amino* radical (NH_2) and the *carboxyl* radical (COOH); *e.g.*,



$$\begin{array}{ccccccc} & & H & & & & \\ & & | & & & & \\ H & — & C & — & NH_2 & & \\ & & | & & & & \\ O & = & C & — & O & — & H \end{array}$$

glycine
(amino-acetic acid)

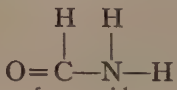


$$\begin{array}{ccccccc} & & H & & & & \\ & & | & & & & \\ H & — & C & — & H & & \\ & & | & & & & \\ H & — & C & — & NH_2 & & \\ & & | & & & & \\ O & = & C & — & O & — & H \end{array}$$

alanine
(amino-propionic acid)

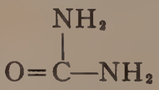
Since the amino radical has basic properties and the carboxyl radical has acid properties, the amino-acids act as *both acids and bases* (p. 52).

Amides are compounds containing the radical $CONH_2$ (*i.e.*, the carboxyl radical with its OH replaced by NH_2); *e.g.*,



$O{=}\overset{\overset{H}{|}}{C}{-}\overset{\overset{H}{|}}{N}{-}H$

formamide



$O{=}\overset{\overset{NH_2}{|}}{C}{-}NH_2$

urea
(carbamide, or
amino-formamide)

The amides act as neither acids nor bases, but are practically non-electrolytes.

Sulphur compounds.—Most of the sulphur-containing organic compounds of biological importance contain the *sulph-hydryl* radical (SH) or the *disulphide* radical (SS) (see pp. 53, 105).

Phosphorus compounds.—Most of the phosphorus-containing organic compounds of biological importance contain the *phosphate* radical (PO_4); *i.e.*, they are *esters* of phosphoric acid (see p. 50).

The relatively simple types of organic compounds discussed in the preceding paragraphs occur in living organisms chiefly as component radicals, and as intermediate products in the synthesis and decomposition, of more complex substances, such as *carbohydrates*, *lipins*, and *proteins*. The composition of these more complex organic compounds is discussed and illustrated by structural formulas in Chapter III.

APPENDIX III

BIBLIOGRAPHY

THE following brief list of references makes no attempt at comprehensiveness, but merely lists a few of the works which the author has found most useful as sources of facts, ideas, and further references. The list is limited to books in English, with the exception of a few journal articles of general nature on important subjects which have not yet been treated in book form. Many of these books contain extensive bibliographies of the original literature.

The titles are grouped according to the chapters of this book with whose subject matter they chiefly deal. To avoid frequent repetitions of titles, they are numbered consecutively and subsequent references are made by referring back to these numbers. Symposium books are listed under the names of their editors. In only a few cases, where it seemed quite essential, have particular chapters or parts of books been indicated in the references.

CHAPTER I

1. MILLS: *The Realities of Modern Science*. New York, 1919.
2. RUSSELL: *The A B C of Atoms*. New York, 1923.
3. GRAY: *The Chemistry Tangle Unravelled*. New York, 1923.
4. LEWIS: *Valence and the Structure of Atoms and Molecules*. New York, 1923.

CHAPTER II

5. WILSON: *The Cell in Development and Heredity*. New York, 1925.
6. SHARP: *Introduction to Cytology*. New York, 1921.
7. AGAR: *Cytology*. New York, 1920.
8. STRASBURGER et al.: *Textbook of Botany*. New York, 1912.
9. COULTER et al.: *Textbook of Botany*. New York, 1910.
10. GANONG: *Textbook of Botany for Colleges*. New York, 1927.
11. SMITH et al.: *Textbook of General Botany*. New York, 1929.
12. PARKER and HASWELL: *Textbook of Zoology*. New York, 1910.
13. SHULL: *Principles of Animal Biology*. New York, 1924.

CHAPTER III

14. HACKH: *Chemical Dictionary*. Philadelphia, 1929.
15. HILDEBRAND: *Principles of Chemistry*. New York, 1928.

16. **Michaelis**: *Hydrogen Ion Concentration.* Baltimore, 1926.
17. **Clark**: *The Determination of Hydrogen Ions.* Baltimore, 1923.
18. **Lowy** and **Harrow**: *Introduction to Organic Chemistry.* New York, 1924.
19. **Bodansky**: *Introduction to Physiological Chemistry.* New York, 1927.
20. **Cameron**: *Textbook of Biochemistry.* New York, 1929.
21. **Gortner**: *Outlines of Biochemistry.* New York, 1929.
22. **Thatcher**: *Chemistry of Plant Life.* New York, 1921.
23. **Haas** and **Hill**: *Chemistry of Plant Products.* New York, 1928.

CHAPTER IV

24. **Bayliss**: *Principles of General Physiology.* New York, 1918.
25. **Fonder**: *Essentials of General Physiology.* New York, 1929.
26. **Findlay**: *Physical Chemistry for Students of Medicine.* New York, 1924.
27. **Bogue**: *Colloidal Behavior.* New York, 1924.
28. **Loeb**: *Proteins and the Theory of Colloidal Behavior.* New York, 1922.
29. **Alexander**: *Colloid Chemistry;* Volume II, Biology and Medicine. New York, 1928.
30. **Cowdry**: *General Cytology.* (Chicago, 1924.) Section V: **Chambers**: The Physical Structure of Protoplasm.

CHAPTER V

31. **Findlay**: *Osmotic Pressure.* New York, 1919.
30: Section III: **Jacobs**: Permeability of the Cell to Diffusing Substances.
32. **Osterhout**: *Injury, Recovery, and Death in Relation to Conductivity and Permeability.* Philadelphia, 1922.

CHAPTER VI

33. **Waldschmidt-Leitz**: *Enzyme Actions and Properties.* New York, 1929.
34. **Waksman** and **Davison**: *Enzymes.* Baltimore, 1926.
35. **Falk**: *Chemistry of Enzyme Actions.* New York, 1924.

CHAPTER VII

36. **Calkins**: *Biology of the Protozoa.* Philadelphia, 1926.
37. **Minchin**: *Introduction to the Study of the Protozoa.* New York, 1922.
38. **Dakin**: *Oxidations and Reductions in the Animal Body.* New York, 1922.
19, 20.

CHAPTER VIII

8, 9, 10, 11, 22, 23.
39. Spoehr: *Photosynthesis.* New York, 1926.
40. Kostychev: *Plant Respiration.* Philadelphia, 1927.

CHAPTER IX

41. Marshall: *Microbiology.* Philadelphia, 1917.
42. Harden: *Alcoholic Fermentation.* New York, 1923.
43. Buchanan: *Bacteriology.* New York, 1924.
44. Jordan: *General Bacteriology.* Philadelphia, 1924.

CHAPTER X

45. Waksman: *Principles of Soil Microbiology.* Baltimore, 1927.
46. Russell: *Soil Conditions and Plant Growth.* New York, 1927.

CHAPTER XI

8, 9, 10, 11.
47. Ganong: *The Living Plant.* New York, 1922.
48. Stevens: *Plant Anatomy.* Philadelphia, 1924.
49. Haberlandt: *Physiological Plant Anatomy.* New York, 1914.
50. Duggar: *Plant Physiology.* New York, 1927.
51. Pfeffer: *Physiology of Plants.* New York, 1900.
52. Palladin: *Plant Physiology.* Philadelphia, 1926.

CHAPTER XII

12, 13, 19, 20, 24, 25.
53. Sedgwick and Wilson: *General Biology.* New York, 1914.
54. Rogers: *Textbook of Comparative Physiology.* New York, 1927.
55. Holmes: *Biology of the Frog.* New York, 1916.
56. Martin: *The Human Body.* New York, 1928.
57. Schafer: *Essentials of Histology.* Philadelphia, 1920.
58. Bailey: *Textbook of Histology.* New York, 1923.
59. Starling: *Principles of Human Physiology.* Philadelphia, 1926.
60. Sherman: *Chemistry of Food and Nutrition.* New York, 1927.
61. Lusk: *Elements of the Science of Nutrition.* Philadelphia, 1923.
62. Macleod: *The Fuel of Life.* Princeton, 1928.
63. Pryde: *Recent Advances in Biochemistry.* Philadelphia, 1928.
64. Evans: *Recent Advances in Physiology.* Philadelphia, 1926.

65. Henderson: *Blood.* New Haven, 1928.
66. Cushny: *The Secretion of the Urine.* New York, 1926.

CHAPTER XIII

67. Lillie: *Protoplasmic Action and Nervous Action.* Chicago, 1923.
68. Parker: *The Elementary Nervous System.* Philadelphia, 1919.
24, 36, 49, 53, 54.

CHAPTER XIV

24, 25, 59, 64.
69. Hogben: *Comparative Physiology.* New York, 1926.
70. Hill: *Muscular Activity.* Baltimore, 1926.
71. Hill: *Living Machinery.* New York, 1927.
72. Hill: *Muscular Movement in Man.* New York, 1927.
73. Meyerhoff: *Chemical Dynamics of Life Phenomena.* Philadelphia, 1924.
74. Harvey: *The Nature of Animal Light.* Philadelphia, 1920.
75. Hogben: *The Pigmentary Effector System.* London, 1924.

CHAPTER XV

24, 57, 58, 59.
76. Parker: *Smell, Taste, and Allied Senses in the Vertebrates.* Philadelphia, 1922.
77. Maxwell: *Labyrinth and Equilibrium.* Philadelphia, 1923.

CHAPTER XVI

24, 25, 54, 57, 58, 59, 63, 67, 68, 69.
78. Lucas: *The Conduction of the Nervous Impulse.* New York, 1917.
79. Ranson: *Anatomy of the Nervous System.* Philadelphia, 1926.
80. Sherrington: *The Integrative Action of the Nervous System.* New York, 1926.
81. Hogben: *Comparative Physiology of Internal Secretion.* Cambridge, England, 1927.
82. Schafer: *The Endocrine Organs.* New York, 1926.
83. Cannon: *Bodily Changes in Pain, Hunger, Fear, and Rage.* New York, 1920.

CHAPTER XVII

8, 50, 52.
84. Holmes: *The Evolution of Animal Intelligence.* New York. 1911.
85. Loeb: *Forced Movements, Tropisms, and Animal Conduct.* Philadelphia, 1918.

86. Pavlov: *Lectures on Conditioned Reflexes.* New York, 1928.
87. Watson: *Psychology from the Standpoint of a Behaviorist.* Philadelphia, 1919.

CHAPTER XVIII

5, 6, 7, 30 (Section V).

CHAPTER XIX

5, 6, 7, 8, 9, 10, 11, 36, 37.

CHAPTER XX

5, 6, 7, 12, 13, 53, 54, 55, 56.

88. Loeb: *Artificial Parthenogenesis and Fertilization.* Chicago, 1913.
89. Korschelt and Heider: *Textbook of Embryology.* New York, 1900.
90. Balfour: *Comparative Embryology.* New York, 1881.
91. Jenkinson: *Vertebrate Embryology.* New York, 1925.
92. Morgan: *The Development of the Frog's Egg.* New York, 1897.
93. Morgan: *Regeneration.* New York, 1921.

CHAPTER XXI

5, 6, 7, 8, 9, 10, 11.

CHAPTER XXII

94. Morgan, Sturtevant, Muller, and Bridges: *The Mechanism of Mendelian Heredity.* New York, 1923.
95. Morgan: *The Physical Basis of Heredity.* Philadelphia, 1919.
96. Morgan: *The Theory of the Gene.* New Haven, 1926.
97. Morgan, Bridges, and Sturtevant: *The Genetics of Drosophila.* The Hague, 1925.
98. Babcock and Clausen: *Genetics in Relation to Agriculture.* New York, 1927.

CHAPTER XXIII

94, 95, 97.

99. Morgan: *Experimental Embryology.* New York, 1927.
100. Goldschmidt: "The Gene." *Quarterly Review of Biology,* Volume 3; 1928.
101. Goldschmidt: *The Mechanism and Physiology of Sex Determination.* New York, 1923.
102. De Beer: *Experimental Embryology.* New York, 1926.
103. Spemann: "Some Factors of Animal Development." *British Journal of Experimental Biology*, Volume 2; 1925.

CHAPTER XXIV

94, 95, 96, 97, 98.

104. MULLER: "The Production of Mutations by X-rays." *Proceedings of the National Academy of Sciences*, Volume 14; 1928.

105. STURTEVANT: *An Analysis of the Effects of Selection.* Carnegie Institution of Washington, 1918.

106. EAST and JONES: *Inbreeding and Outbreeding.* Philadelphia, 1919.

107. YULE: *Introduction to the Theory of Statistics.* Philadelphia, 1911.

108. FISHER: *Statistical Methods for Research Workers.* London, 1928.

CHAPTER XXV

109. DARWIN: *The Origin of Species.* London, 1859.

110. MORGAN: *Evolution and Genetics.* Princeton, 1925.

111. STURTEVANT: *The North American Species of Drosophila.* Carnegie Institution of Washington, 1921.

CHAPTER XXVI

109, 110.

112. ROMANES: *Darwin and After Darwin.* Chicago, 1892.

113. NUTTALL: *Blood Immunity and Blood Relationship.* Cambridge, England, 1904.

114. PIRSSON and SCHUCHERT: *Textbook of Geology;* Part II, Historical Geology. New York, 1915.

115. SHIMER: *Introduction to the Study of Fossils.* New York, 1914.

116. SWINNERTON: *Outlines of Paleontology.* New York, 1923.

117. ZITTEL: *Textbook of Paleontology.* New York, 1902.

118. WALLACE: *The Geographical Distribution of Animals.* New York, 1876.

119. WILLEY: *Amphioxus and the Ancestry of the Vertebrates.* New York, 1894.

120. WILDER: *The History of the Human Body.* New York, 1923.

CHAPTER XXVII

29: Chapters 1, 27, 28.

121. MULLER: "The Gene as the Basis of Life." *Proceedings of the International Congress of Plant Sciences*, Volume 1; 1929.

INDEX

INDEX

The numbers in bold-face type serve the purpose of a glossary, referring to pages containing definitions, formulas, or extensive discussions. Italic numbers refer to pages containing illustrations. Words in italics are the scientific names of taxonomic groups (species, genera, etc.).

Aberrations, 494, 531, *532*, 557, **559**, *564*, *566*; relation to interspecific sterility, 611, 616.
Absorption, **91**, 111, 124, 170, 183, 186, 191, 205, 235.
Acanthocephala, **671**.
Accessory nutritive processes, **107**.
Acetic acid, **113**, 142, **683**; aldehyde, **113**, 138, **683**.
Achromatium, *153*.
Acidic, **43**, 681.
Acids, 43, 44, 52, 94, 95, 97, 272, **680**.
Acquired characters, inheritance, **574**, 617.
Acrosome, *387*.
Actinozoa, **671**.
Action current, **238**, 239, 265, 282, 293.
Activation, 378, **391**, 392, 415; artificial, 391, 418; by foreign sperm, 543.
Adaptation, **597**–601.
Adaptive characters, 626.
Adhesion, 12, **13**.
Adrenal glands, 323; cortex, 329.
Adrenalin, 322, **323**, 324, 325
Adsorption, **67**, 72.
Aeration, of blood, 207, 223; system (plant), *181*.
Afferent fibers, **254**, *255*, *257*, 301.
Air, 149, 225.
Alanine, **53**, **113**, 684.
Albinism, **520**.
Albumins, **54**.
Alcoholic fermentation, **138**.
Alcohols, 131, **682** (*see* Ethyl alcohol).
Aldehydes, 683.
Algae, **31**–36, **122**, 156, 183, 245, 288, 424, 426, 450; blue-green, *29*, 667, 669; brown, 123, 160, 376, 426, 670; colonial, 124; green, *123*, 669; red, 123, 376, 426, 670.
Alkaloids, **131**.
Allantois, **403**, 404.
Allelomorphs, **464**, 469, 470, 472, 478, 483, 486, 488, 567, 569, 570, 571.
All-or-none law, 242, **243**, 262.
Alternation of generations, **376**, 423.
Aluminum, **39**; atom, *8*.
Alveolar air, 225, 226.
Alveoli, **224**, *225*, 226.
Amicroscopic particles, **61**, **62**.
Amides, **685**.
Aminases, **106**.
Amination, **106**.
Amines, 204, **684**.
Amino radical, **51**, 52, 106, **684**.
Amino-acids, **51**–55, 63, 78, 86, 104, 203, 205, 213, 231, 513, **684**; dissociation, 52; metabolism, 114, 214, 220; synthesis, 116, 128, 177, 220.
Amitosis, **360**, *361*.
Ammonia, **42**, 52, 86, 91, 106, 114, 139, 144, 149, 150, 204, 215, 229, **684**; molecule, *10*.
Ammonium hydroxide, **43**, **684**; ion, **42**; salts, 128; sulphate, **136**.
Amnion, **403**.
Amoeba, 28, *30*, 108, *109*, 121, 244, 272, 334, 670; division, *363*; evolution, 667.
Amoeboid movement, 249, 259, **272**.
Amphibia, 196, 232, 345, 383, 388, **673**; circulation, 209; development, *399*, 544; metamorphosis, 328, **407**; phylogeny, *651*.
Amphineura, **672**.
Amylase, **104**, 111, 177, 536.
Amyloplasts, **179**.
Amylopsin, **203**, 205.
Anabolism, **112**.
Anaerobes, facultative, **143**; obligatory, 143.
Anaesthetics, 87, **240**, 245.
Analogous organs, **625**.
Anaphases, **352**, 358.
Andalusians, 459, 462.
Angiosperms (*Angiospermae*), **670**; reproduction, 434–*438*–441.
Animals (*Animalia*), 30, 36, **670**; nutrition, **108**–121, 184–235; origin, 666; reproduction, 380–422.

Anions, **9**, 42, 52, 71, 86.
Annelids (*Annelida*), 420, **672**; phylogeny, *648*.
Annual rings, 446.
Annulata, **672**.
Antheridia, **427**, *428*, 430, *431*.
Anthers, **436**.
Anthozoa, **671**.
Antibodies, **634**.
Antigens, **634**, 635.
Antipole, **544**, *547*.
Ants, 345, 388, 405, 416, 613.
Anus, 191, 206; development, 395, 400.
Aorta, *208*.
Aortic arches, *192*, 193, *208*.
Ape-men, 652.
Apes, 346, 634, 652, 674.
Aphids, 417, 418, 505, 508.
Apical cell, 159, *161*, **442**.
Apogamy, **449**, 508.
Apospory, **450**, 508.
Arachnida, **672**.
Archegonia, **427**, *428*, 430, *431*.
Archeozoic era, 638, *639*.
Archiannelida, **672**.
Arginine, **53**.
Armadillo, polyembryony, 419.
Arteries, *206*, **207**, *208*, 209.
Arthropods (*Arthropoda*), 256, 290, 345, 421, 503, **672**; phylogeny, *648*.
Ascaris, 410.
Ascomycetes, 670.
Aspartic acid, **53**.
Aspergillus, *137*, 670.
Assimilation, 4, 21, 23, 55, 117, 130, 180, **350**.
Asteroidea, **672**.
Asters, **353**, 358, 360, 389, *390*.
Atmosphere, **173**.
Atomic number, **9**.
Atoms, 6, *8*, 12, 44; size, 62; symbols, 675.
Auricles, 207, *208*, 209.
Australian region, *645*, 646.
Autocatalysis, 516, 537, 658, 660, 661, **662**, 663, 667.
Autonomic ganglia, **310**; nervous system, *311*; neurones, 313.
Autosomes, *497*, **498**; rôle in sex-determination, 502, 562, 563.
Autotrophic, **144**; bacteria, **144**.
Auxocytes, **410**, 411, 487.
Aves, **673**.
Axial filament, **271**, *387*.
Axon, **253**, 301.

Bacilli, *142*.
Back-cross, *468*, **469**, 475, *476*, 479, *480*, 482, *484*, 489.
Bacteria, **29**, 31, 36, **141**, *142*, 669; anaerobic, **143**, 148; autotrophic, **144**, 150, 666; colonies, 33, 34; denitrifying, **150**; division, 359, 509; evolution, 665, 667; heredity, 509; intestinal, 204, 206; nitrate, **150**, *151*; nitrifying, **150**, *151*; nitrite, **150**, *151*; nitrogen-fixing, **151**, *152*; nutrition, **141**; origin, 656; parasitic, **143**; pathogenic, **143**; putrefactive, 142, 150; rate of multiplication, 590; reproduction, 369; saprophytic, **142**; size, *17*; spores, 366, 378; structure, 16, 22, **29**, 656; sulphur, 144, *153*.
Bacteriophage, **143**.
Balanoglossus, 650, 673.
Bases, 44, 52, **680**.
Basic, **43**, **681**.
Basidiomycetes, 670.
Bast, **167**; fibers, *165*, **167**.
Beans, 444; germination, *445*; selection, 581; size, frequency-distribution, *577*.
Bees, 345, 388, 405, 416, 505.
Behavior, **333**, 598; modification, 305, **341**.
Bicarbonates, 227, **681**.
Bile, **203**, 234; duct, *197*, *200*; pigments, ~~204,~~ 206, **210**, 234; salts, 99, **204**, 215.
Binary fission, **363**.
Binomial names, **37**.
Bioelectric currents, 14, **239**.
Biology, **3**; central problem, 667; fundamental postulate, **15**.
Birds, 196, 215, 232, 281, 345, 383, 385, 388, 402–405, 504, 612, *624*, *633*, 635, 651, **673**.
Bivalents, **411**, *412*, 486.
Blastocoel, **394**, *397*, *399*.
Blastopore, **395**, 398, *399*; dorsal lip, **546**, *547*, *548*.
Blastula, *393*, **394**, *395*, *547*.
Blood, 85, 191, 194, 198, 206, **210**, 226, 321, 398; cells, 191, 195, 210, 401; clotting, **211**; corpuscles, 84, *210*, 228; immunity reactions, 634; plasma, 191, 210, **211**, 228, 231; pressure, 207, 233; relationships, 634, 635; vessels, *190*, 191, *192*, 198, **206**, 401.
Body cavity, **189**, 196; fluids, **35**, 39, 41, 78, 81, 84, 86, 90, 107, 187, 189, 321, 666; temperature, 50, **218**, 281; wall, **189**, 196, 396, 400.
Bones, 42, 196, 198, 261, 327, 398, *624*.
Boron, **39**; atom, *8*.
Brachiopoda, **672**.
Brain, 219, 256, 258, **307**, *308*, *309*, 400; stem, **309**.

Breathing, **225**.
Breeding habits, **387**.
Bromine, **39**.
Bronchi, *200*, **224**.
Bronchioles, **224**, *225*.
Brownian movement, 62, 64, 71, 75, 76, 274.
Bryophytes (*Bryophyta*), 160, **670**; growth, **442**; phylogeny, *648*; reproduction, 423, **427**, 451; sex-determination, 505, *506*.
Bryozoa, 420, 421, **672**.
Budding, **364**, 415, **419**, *420*, 429, 449, 450.
Buds, **446**, *447*; lateral, **447**, 552; terminal, **447**, 552; winter, 446.
Buffers, **43**, 55.
Bulbils, **451**.
Bulbs, **451**, 584.

Calciferous glands, **190**, 252.
Calcium, **39**, 154, 222, 327; atom, *8*; carbonate, 42; ion, **42**, 69, 86, 89, 263, 327; oxalate, 133, 182; phosphate, 42, 122, 136, 327; salts, 240, 327.
Calorie, **112**.
Calyx, **434**.
Cambium, *163*, *164*, *165*, **166**, 167, 446.
Cambrian period, 640, 649.
Capillaries, 193, *206*, **207**, *208*.
Capillary force, 171, **173**; water, **171**.
Carbohydrases, **104**.
Carbohydrates, 25, **46**, 56, 104, 108, 154, 685; fuel value, 114, 218; metabolism, **112**, 214, 325; synthesis, **124**.
Carbon, 11, **39**, 42, 45, 46, 48, 51, 102; atom, *8*; chemical properties, **44**; cycle, 146; dioxide, **42**, 102, 113, 120, 122, 124, 147, 176, 194, 225–228, 268–270, 296, 330.
Carbonate, 43, 44, 147, **171**, **681**; ions, **42**.
Carbonic acid, **43**, 681.
Carboxyl radical, **51**, 679, **683**, 684.
Carboxylases, **106**.
Carnivora, 651, **674**.
Carpels, **435**, 436, 440.
Cartilage, 28, 196, 198, 398.
Catabolism, **112**.
Catalase, **105**, 143.
Catalysis, **94**.
Catalysts, **94**, 535–537, 540, 550, 556.
Cations, **9**, 42, 71, 86.
Cell division, 19, *21*, 33, 90, 350, **351**; membranes, 16, *19*, *20*, **27**, 31, 78, 83, 85, 87, *110*, 238; plate, **353**; sap, **26**, 87, 90; wall, *18*, *23*, **27**, 30, *31*, *33*, *82*, 87, *123*, 353, 665.
Cells, 3, **16**, *18*, *19*, *20*; evolution, 665; form, **17**; interrelations in the multicellular organism, **35**; osmotic pressure, 81; size, 16, *17*; structure, 18.
Cellulose, 27, 30, **46**, 47, 48; synthesis, 131.
Cenozoic era, *639*, 640.
Central nervous system, **252**, 300, *308*; conduction paths, *315*; development, 398, 546; structure, **307**.
Centrolecithal eggs, **385**, *386*.
Centron, **305**.
Centrosome, **354**, 358.
Cephalization, **256**, **258**.
Cephalochorda, 649, 651, **673**.
Cephalopoda, **672**.
Cerebellum, *308*, *309*, **310**, 318, 319, 320.
Cerebrum, *308*, *309*, **310**, 318, 319, 320, 344, 345.
Cestoda, **671**.
Cetacea, 651, **674**.
Chaetognatha, 650, **671**.
Chaetopoda, **672**.
Chemical affinity, **13**, 67, 95; change, 6, **12**; characters, 633; combination, 6, 9, 56; equations, **679**, 680; symbolism, **675**.
Chemical reactions, 13, **679**; in organisms, 93, **100**; rate (velocity), **11**, 95, 540, 550; reversibility, **96**.
Chemo-receptors, **286**.
Chemotropism, **336**, 338, 427, 430.
Chiroptera, 651, **674**.
Chlamydomonas, *123*, 367, 669; reproduction, 371, *372*.
Chlorenchyma, **168**, 169.
Chloride ion, **42**.
Chlorine, 39, 154, 222; atom, *8*; molecule, *10*.
Chlorophyceae, **669**.
Chlorophyl, 31, 122, **126**, 445, 509; absorption spectrum, *125*; evolution, 665, 666; synthesis, 131.
Chloroplasts, *18*, **25**, *31*, *33*, *123*, 126, *157*, *168*, 176, 510, 660.
Cholesterol, 48, **51**, 402.
Choline, 50, **684**.
Chondriosomes, **25**.
Chordata, 641, **672**; phylogeny, *648*, 649, 650, *651*.
Chorion, **386**.
Chromaphil cells, **323**.
Chromatin, 16, **20**, 351, 355, 373, 386, 454, 516, 656, 660; chemical composition, **55**, 512; volume, 514.
Chromatophores, 242, **279**.
Chromidia, **22**, *29*, 30.
Chromosomes, 19, **21**, 22, 73, **351**,

352, 357, 358, *493*, 513, *521*, 555, *561*, *562*; aberrations, 559; attachment, 559, *564*, 565; division, 352, 355, 356, 391, 455; elimination, *532*, 534, 543, 559, 563, 565; fragmentation, 559, 565; homologous, 411; in foreign cytoplasm, 543; in heredity, 454–521; in species hybrids, 610; individuality, 356, 454; length, 494; maps, *492*, 493, 494; non-disjunction, 563; number, 351, 355, 356, 374, 377, 391, 413, 479.
Cilia, 31, 109, *110*, 188, 245, 251, 270, *271*, 334.
Ciliary movement, 270, *271*, 298.
Ciliates, 31, 245, 298, 370, 378.
Circulation, *192*, 206, *208*.
Circulatory system, 191, 198, 206, 398.
Class, 36.
Classification, 36, 620, 669; natural, 620, 622.
Cleavage, *393*, 394, 528, 529, 546, 553, 554.
Climate, 594; changes, 602.
Cloaca, *197*, 201, 233, *383*.
Clone, 584.
Closterium, *123*, 669.
Coagulation, 74, 99.
Coarse particles, 60, 61, 62.
Cocci, *142*.
Cochlea, 286, *287*.
Coelenterates (*Coelenterata*), 298, 335, 345, 396, 398, 419, 420, 553, 671; phylogeny, *648*, 649.
Coelom, 189, *196*, 384; development, 396, *397*, *399*, 400, 650.
Coelomic fluid, 189, 195; pouches, *393*, 396.
Cohesion, 13, 41, 59, 65, 72.
Colloidal dispersions, 60, 70; emulsions, 70, 88; ions, 81; molecules, 76, 89; particles, 61, 62, 76; solutions, 63, 70, 71; suspensions, 70.
Colloids, 63, 78, 81, 85, 98; hydrophile, 70; hydrophobe, 70.
Colonial organisms, 33, 124, 364, 367, 665.
Color, 126.
Competition, 594, 603, 614.
Components, 6.
Compounds, 6, *7*; classification, 680; in organisms, 40; inorganic, 9, 40, 44, 680; nonpolar, 10; organic, 44, 680; polar, 9; polar-nonpolar, 11.
Concentration, 76, 78, 81, 82, 84, 87, 95, 96, 100.
Condensation (chemical), 103, 127.
Conductors, 243.
Cones, 289, *291*.
Conjugatae, 369, 370.
Conjugation, 369, 370, 378.
Connective tissues, 198, *201*, 398.
Consciousness, 348.
Constituents, 6.
Contraction period, 264, 270.
Coordination, 212, 249, 293, 597; chemical, 293, 321; developmental, 551–553; nervous, 293, 332.
Copper, 39; ferrocyanide, 78.
Copulation, 388.
Corn, *164*, 437, 530, 536, 586.
Cornea, 289, *290*.
Corolla, 434.
Cortex, *163*, *165*, 166, *171*, 178, 446.
Cotyledons, 437, *438*, *443*, *445*, 466.
Crabs, 329, 345, 672.
Cranial nerves, 314.
Crenation, 83.
Crinoidea, 672.
Crocodiles, 651, 673.
Cross-fertilization, 387, 581, 584–586; -pollination, 437, 581.
Crossing-over, 413, 457, 483–*486*–496, 521, 566; double, *491*, 493, 495; frequency, 488, 491, 494, 496.
Crossopterygii, 651, 673.
Cross-over value, 489, 493, 495.
Crustacea, 405, 416, 672.
Crystalloidal molecules, 76; particles, 61, 62; solutions, 60, 63.
Crystalloids, 63, 78, 85–89, 98.
Ctenophora, 671.
Cyanophyceae, *29*, 30, 36, 141, *359*, 366, 369, 656, 660, 669.
Cyclostomes (*Cyclostomata*), 651, 673.
Cystine, 53.
Cysts, 366.
Cytochrome, 105.
Cytoplasm, 4, 16, *18*, *19*, *20*, 24, 354, 655; evolution, 665, 666; functions, 24; relation to genes, 517, 543; rôle in development, 525, 541.
Cytoplasmic inheritance, 509, 542.

Darwin, 614, 616, 618, 637.
Datura, *561*.
Deamination, 106, 114, 214, 220.
Death, 87, 89.
Decarboxylation, 106, 112.
Decay, 142.
Deficiency, 560, 565, *566*.
Degeneration of useless organs, 627, 628.
Dehydrogenation, 102, 104, 105.
Dehydrolytic synthesis (*see* Synthesis).
Dendrites, 253, *255*, 301.
Deoxygenation, 102.
Desaturation, 216.
Determination, developmental, 547–554; genetic, 465.

Development, **349**, **517**; factors, 452, 524; mechanism, **524**; of animals, **392**, *393*, *397*, *399*; of plants, **440**, *443*, *445*, *447*; regulation, 551–553.
Developmental characters, 630.
Dextrins, **47**.
Dextrose, **677**.
Diabetes, **325**.
Dialyzing membranes, **63**, 70, 78, 85, 98.
Diatoms, 376, 377, 669.
Dicotyledons (*Dicotyledoneae*), *163*, *164*, *165*, *181*, *443*, 446, *447*, **670**.
Differentiation, chemical, 549, 553; factors, 554; intercellular, 35, 156, 355, 366, 442; intracellular, 31; mechanism, **544**.
Diffusion, 35, 70–72, **75**–92, 111, 120, 267, 404, 552; law, **76**; medium, 76; rate, **76**.
Digestion, 101, **110**, 186, 187, 191, **201**, 235; extracellular, **139**; in plants, 131, 177.
Digestive enzymes, **104**; glands, 198, 398, 401; organs, 189, 197, 201, 398; system, 104, *191*.
Dioecious, **373**, 380, 496.
Dionaea, 245.
Dioptric mechanism, **289**.
Diploid, **374**, 391, 411, 423, 450, *493*, *561*, *562*, 563.
Dipnoi, 651, 673.
Disaccharoses, **46**, 94, 96, 101.
Disease, 140; germs, **143**.
Dispersed particles, **60**, 63, 70, 72, 73.
Dispersion medium, **60**.
Dispersions, **59**, 63, 72.
Dissociation, **10**, 40; of water, **41**, 43.
Distribution (of food), 159, 160, 162, 163, 172, 177, 183, 188, 191, 193, 212, 213, 235.
Dominance, **469**.
Dominant, **465**, *466*–470, 532, 568, 587.
Drosera, 245.
Drosophila, **479**, 672; aberrations, 561–566; chromosome maps, *492*; chromosomes, 479, *493*, *497*, *564*; development, 531; genes, 514; heredity, **479**–*480*–*484*–*500*–503, 511, 518; mosaics, 532–*533*–534; mutations, 568–570, 598, 607, 608, 627; rate of multiplication, *592*.
Dryopithecus, 652.
Ductless glands, **322**.
Ducts, *165*, **166**, 172, 173, 446.
Duplication, 560, **565**, *566*.

Ear, 285, *286*.
Earthworm, **188**, *190*, *192*, 672; development, 396, *397*, 402; nutrition, 189–195, 235; reproduction, 388; responsive mechanisms, **251**, *253*, *255*.
Echinoderms (*Echinodermata*), 385, 419, 421, 503, 553, **672**; phylogeny, *648*, 650.
Echinoidea, **672**.
Ecological factors, **642**.
Ectoderm, **185**, *189*, **395**, *397*, 398, *399*, 545, 546.
Ectoplasm, **24**, *30*, 31, 73.
Edentata, 646, 651, **674**.
Effectors, **243**, 257, **259**; independent, **249**, 252, 258, 263, 276; mechanical, **259**; pigmentary, **279**.
Efferent fibers, **254**, *255*, *257*.
Egestion, 75, 111, 186, 188, 191, 205, 235.
Egg-cell, 17, *372*, **373**, 381, 385, *386*, 415, *428*, *431*, 436, *438*, *547*; axes, **545**, **546**, *547*; polarity, **545**; symmetry, **545**, **546**.
Elaioplasts, **179**.
Elasmobranchs (*Elasmobranchii*),651, **673**.
Electric charge, **7**, 13, 267; currents, **12**, 13, 14, **239**, 294; double layer, **238**; fishes, 14, 280; gradients, 549, 552; organs, 242, **280**; phenomena in absorption and secretion, 92; potential, **238**, 278, 549, 552; response, **238**, 265, 270, 278, 389.
Electricity, negative, **6**; positive, **6**.
Electrolytes, **10**, 70, 81; strong, 10, 41, **63**, 681; weak, 10, **63**, 681.
Electromotive force, 239, 280.
Electrons, **6**, 12, 573; planetary, **7**; valence, **9**, 44.
Electrostatic attraction, **7**, 9, 10, 12, 67, 71; repulsion, **7**, 12.
Elements, **6**; chemical properties, **9**; electro-negative, **9**; electro-positive, **9**; free, **6**, *7*; in foods, 39, 146; in organisms, **39**; inert, **9**; metallic, **9**, 44; non-metallic, **9**, 44.
Elephant, rate of multiplication, 590.
Elodea, *18*.
Embryo, **392**, *393*, *397*, *399*, *428*, *431*, *433*, 437, *438*, *443*, 526, 530, *547*, *633*; differentiation, 544; double, *548*; median plane, **546**; nutrition, **401**; rotation, *547*.
Embryonic membranes, **403**, 631; structures, 631, 632.
Embryo-sac, *435*, **436**, *438*.
Emotions, 323.
Emulsifying agents, **67**.
Emulsions, **60**, **63**, 67–*69*, 76, 88.
Endocrine organs, **322**, 332.
Endoderm, **185**, *189*, **395**, *397*, 398, *399*, 545, 547.

Endodermis, *165*, **166**.
Endoplasm, **24**, *30*, 31, 72.
Endosperm, **437**, *438*, 439, **444**; nucleus, **437**.
Energy, **6**, **12**, 90, 94, 97, 102, 107, 118, 278; chemical, **13**, 14, 92, 95, 101, 266; conservation, **13**, 15, 125, 154, 217; degradation, **14**, 15, 155, 281; electrical, **13**, 14; expenditure, **217**; first law, **13**; forms, **13**; in living things, **14**; kinetic, **13**, 92, 236; laws, **13**, 15; mechanical, **13**, 14, 154, 266, 269; molecular, **13**, 75, 92, 234; potential, **13**, 65, 97, 101, 118, 236, 266, 269, 273; quantity, **112**; radiant, 12, **13**, 14, 15, 126, 154, 553; second law, **14**, 155, 280; surface, **65**, 67; transformations, **13**, 15, 65, 154.
Enteron, **184**, *185*, *189*, *196*, 197, *201*, 395, *397*, *399*, 546.
Enteropneusta, **672**.
Environment, 75, **524**; changes, 602–604; external, 526, **539**, **599**; internal, **526**; modifying effect, **539**, **573**, 604, 617; rôle in development, 452, 525, 539, 544–546, **554**; selective effect, **539**, 595, 604, 605.
Enzymes, 23, **97**; classification, **103**; digestive, **104**, 110, 202–**205**; extracellular, **103**; glycolytic, **106**; hydrolyzing, **103**, **104**, 110, 186, 187, 191, 246; intracellular, **103**; mode of action, **99**; nature, **98**; oxidizing, **103**, **104**; production, 99, 350, 535, 536, 556, 663; specificity, **98**.
Eoanthropus, 652.
Epicotyl, *438*, *443*, **444**, *445*.
Epidermal system, *163*, **164**.
Epidermis, 160, 162, *165*, 166, *168*, 169, *171*, 398, 446, 546.
Epithelial cells, 26, 185, 224; tissues, **198**.
Epithelio-muscle cells, 185, *248*, 249.
Epithelium, *275*, *292*; ciliated, 271.
Equational division, **414**, 416, 505.
Equilibrium organs, **285**.
Equisetineae, **670**.
Erepsin, **104**, 204, 205.
Esophagus, 190, *191*, *197*, *200*, 201, 202.
Esterases, **104**.
Esters, 48, 51, 104, **683**.
Ethiopian region, *645*, 647.
Ethyl alcohol, **113**, 138, 142, **682**; molecule, *10*.
Eudorina, 367, *368*; gametes, *372*.
Euglena, *141*.
Eumycetes, **670**.
Eustachian tubes, *286*, 400, 632.
Eutheria, **673**, 674.
Evolution, **619**; mechanism, 590–618; results, 619–653; stages, 665.
Excitation, **238**, 265, 270, 282; transmission, **293**–*295*–299.
Excretion, **91**, **120**, 133, 182, 186, 188, 195, 229, 235.
Excretory organs, 188, 195, 198, 229, 398; pores, *187*, *190*, *194*; system, 187, 383; vessels, *187*, *188*.
Experience, 305, 339, **343**.
Experimental breeding, **457**, 519, 580.
Extinct organisms, 600, **635**.
Extractives, **55**, 56, 63.
Eye, **289**, *290*, 627–629; spot, *123*, *141*, 245, **288**, 629.

Facilitation, **305**, 344.
Family, **37**.
Fat tissue, 198, **214**, 219.
Fatigue, 263, 264, **268**, 272, 304, 342.
Fats, 25, 45, **48**, 63, 108; digestion, 111, **203**, 205; distribution, 213; fuel value, **114**, **218**; metabolism, **114**, 215; storage, 51, 115, 138, 179, 214, 216, 219, 401; synthesis, **116**, 127, 130, 219.
Fatty acids, **48**, 66, 104, 114, 116, 203, 205, 213; saturated, **49**, 216; unsaturated, **49**, 50, 216.
Feces, **205**, 234.
Female, **373**.
Ferns, 430, 670; reproduction, **430**, *431*, 441, 451; stem, *164*.
Fertility, 559, 587, 598.
Fertilization, **369**, 373, *375*, 379, **389**, *390*, 427, *438*, 455, 545; membrane, **389**, *390*.
Fibrils, **26**, 73, 91.
Fibrin, **211**.
Fibrinogen, **211**.
Fibro-vascular bundles, **164**, 168, 172; system, *163*, **164**; tissues, **166**, 446.
Filicineae, **670**.
Filterable viruses, **28**, 143, 517, 657, 661, 665; origin, 659; size, *17*, **658**.
Fishes, 196, 223, 232, 280, 345, 382, 385, 388, 421, 504, 529, 651, **673**; circulation, **207**, *208*; embryo, *633*.
Fission, *363*, 415, **419**, 450.
Fitness, 595, **597**, 600.
Fixation, **18**, *73*, 74, 351.
Flagella, 30, 31, *123*, 140, *141*, 186, 245, 248, **270**, *387*.
Flagellates (*Flagellata*), 36, **140**, *141*, 369, 622, **669**, 670; nutrition, **141**, 145; phylogeny, *648*.
Flame-cells, **188**.
Flatworms, 186, 382, 419, 420, 421, **671**.

Floral envelopes, **434**.
Flower, **434**, 448.
Fluorine, **39**, 222; atom, *8*.
Food, 4, 39, **107**, 540; cycle, **146**, *147*; storage, 162, 163, **178**, 183, 214, 216, **218**; substances, 108, 122; supply, 592, 593.
Forgetting, **305**.
Formaldehyde, 101, 126, 129, **683**.
Formed bodies, **20**, **25**, 72, 91, 101, 357.
Formic acid, 101, **683**.
Formulas, 46, **675**; structural, 46, **676**.
Forward direction, law, **301**, 302.
Fossils, 635–**636**–641, 643, 647, 650, 652, 667.
Four-o'clock, 459, 510.
Fragmentation (chemical), **103**, 106, 112.
Free nerve endings, *257*, **292**.
Frequency-distribution, *577*, **578**; curves, *577*, **578**, *579*, *582*, *585*.
Frog, *197*, 651, 673; circulation, *208*; development, *399*, **544**, *547*, 553; nervous system, *308*; reproductive organs, *383*.
Fructose, **46**, **47**, 94, 104, 205.
Fruit, 178, **439**.
Fucus, 376, 426.
Fuel substances, 47, **112**, 265, 296; values, **112**, 114, 218.
Fundamental system, *163*, **164**.
Fungi, **31–36**, **135**, *137*, 669, 670; nutrition, **139**, 145; reproduction, 424, 426.

Galactose, **46**, 47, 104, 205.
Gall-flies, parthenogenesis, 417, 418.
Galvanotropism, **336**, *337*.
Gametes, **369**–*371*–*372*–376, 381, **385**, *409*, 413, 454, *473*, *477*, *506*.
Gametophyte, **376**, 423–*428*–*431*–*433*–*435*–*438*–441, 449, 450, 505, 529.
Ganglia, **252**, 300; autonomic, **310**, *311*; cerebral, *253*, **256**; parasympathetic, **310**, *311*; peripheral, **310**, 401; sensory, *257*, 258, **310**, *312*, 313; sympathetic, **310**, *311*, *312*.
Ganoids, 651, 673.
Gases, **58**, 78, 86, 88; in organisms, 40, **42**.
Gastric juice, **202**, 205.
Gastropoda, **672**.
Gastrula, *393*, **395**, *397*, *399*, 529, 531, *547*.
Gastrulation, *393*, **395**, *397*, *399*, 546, *547*, 552.
Gelatin, 72, 76, 634.
Gelation, 72, 73.
Gels, 59, 69, 70, **71**, 73, 76; liquefaction, 72, 73.
Gemmae, **451**.
Generative nucleus, *438*, 439.
Genes, **21**, 24, 29, **455**–521; as basis of life, **660**; autocatalysis, **516**, **537**, 660, **662**, 667; composition, **512**, 663, 667; differentiation, 665; division, 356, 358; free, 517, 662; linear order, **489**, 496; mode of action, **535**; mutation, 515, **567**, 662; nature, **512**, 663, 667; number, **514**; origin, **663**, 667; phenotypic effects, **517**, 538; place of action, **531**; plastid, **511**, 660; recombinations, 379, 414, **557**; relation to cytoplasm, 517, 543, 666; rôle in development, 524, **554**; sex-determining, 496–507, 562; sex-linked, **502**–504, 521; size, **514**, 517, 661, 663; stability, 465, 515, 568; structure, 515, 572, 663, 667; time of action, **526**.
Genetic factors, **452**, 524, 554.
Genotype, **470**, 475, 558.
Genus, **37**.
Geographical barriers, **612**, 643; distribution, 612, **642**; isolation, 604, **612**, 643.
Geological changes, **602**; epochs, 652; eras, **637**, *639*; periods, **637**, *639*, 652; strata, **637**; time, **637**, *639*.
Geometrical progression, **591**.
Geotropism, *246*, **336**, 444.
Gephyrea, **672**.
Germ cells, **367**, *368*, 381, **408**, *409*, 448, 452, 454; plasm, **453**.
Germination, 439, **444**, *445*.
Gill arches, **223**, *224*; filaments, **223**, *224*; slits, **223**, *224*, 400, 632, *633*.
Gills, 198, 207, **223**, *224*.
Gland cells, *23*, 26, 186, 195, 246, 248, 275–278, 401.
Glands, 198, 199, *206*, 251, 257, 259, 274, *275*, *277*; ductless, **322**.
Globulins, **54**.
Glomerulus, **230**, 231.
Glottis, *197*, *200*, **224**.
Glucose, 46, **47**, 93, 104, 106, 205, 231, 266, **678**; metabolism, 112, **113**, 114, 131, 138, 214, 219, 325; synthesis, 124, 127, 177.
Glutamic acid, **53**.
Glutathione, **105**.
Glycases, **106**.
Glycerol, 48–51, 63, 83, 104, 205, 213, 682; metabolism, **113**–116.
Glycerose, 113–116.
Glycine, **51–53**, **684**; synthesis, 128–129.

Glycogen, **46**–48, **115**, 138, **214**, **219**, 265–270, 325, 402.
Glycoproteins, **54**.
Glycyl-glycine, **52**.
Golgi bodies, **25**; organ, *284*.
Gonads, *196*, **380**, *381*, 382, *383*, *384*; development, 401, 410; internal secretions, 328, 385, 535.
Gonia, *409*, **410**.
Gonium, 367, 372.
Gonoducts, **382**, 401.
Gradients, electrical, **549**, 552; metabolic, **549**–551.
Grafting, **451**, 508, 584.
Granules, **26**, 91; secretory, **275**.
Gray crescent, **545**, *547*, 548, 551, 554.
Green plants, 15, **122**, 593; nutrition, **122**–*134*, 156–**183**; origin, 666.
Growing point, 159, 167, **442**, *447*, 549.
Growth, 3, 4, 117, 118, 133, 159, 327, **349**, **350**, 440, *447*, 516, 661; movements, *246*, **247**, 273; period, *409*, **410**; stage, **19**.
Guard-cells, *168*, **169**, **174**, *175*.
Gymnosperms (*Gymnospermae*), 434, 443, **670**.
Gynandromorphs, *533*, **534**.

Habit, 305, 320, 339, **343**.
Haploid, **374**, 391, 413, 423, 450, 478, 495, *561*, 563.
Hearing, **286**.
Heart, *197*, 198, *200*, **207**, *208*, **219**, 261, 263, 299, 331.
Heat, 12–14, **62**, 154; capacity, **41**; production, *264*–270, **280**, 296.
Hematin, **54**, 105, 130, 154.
Hemicellulose, **179**.
Hemichorda, 650, 651, **672**.
Hemoglobin, **54**, 55, 191, 194, **210**, 226–228.
Hepatic artery, *208*, **209**; portal system, **209**; vein, *208*, **210**, **213**.
Hepaticae, **670**.
Heredity, 21, **452**, 614; chromosome theory, **458**; in man, **519**; laws, **458**, **464**, **478**, **495**; mechanism, **452**; methods of study, **457**.
Hermaphrodites, **380**, 387.
Heterotrophic, **145**.
Heterozygous, **464**, 467, 468, 489, 496.
Hirudinea, **672**.
Histidine, **53**.
Holophytic, **122**, **144**.
Holothuroidea, **672**.
Holozoic, **108**, **145**.
Homo heidelbergensis, 652; *neanderthalensis*, 652; *sapiens*, 652, **653**.
Homolecithal eggs, **385**, *386*, 394.
Homologous chromosomes, **411**, 457, 460, 472, 478, 479, 483, 486, 491, 567, 610; organs, **623**, *624*.
Homozygous, **464**, 467, 468, 489, 496, 583, 586.
Hormones, **321**.
Host, **140**.
Hunger, **285**.
Hybrids, interspecific, **529**, 609, 610, 615.
Hydra, **184**, *185*, *189*, 671; budding, *420*; nutrition, 186, 235; reproductive organs, *381*; responsive mechanisms, **247**, *248*, *250*, 298, 299.
Hydration, 60, **62**, 64, 70, 72, **102**, 104, 112.
Hydrocarbon radicals, **45**.
Hydrocarbons, 66, 147, **681**, **682**.
Hydrochloric acid, 99, **202**; molecule, *10*.
Hydrogen, 11, **39**, 41, 45, 46, 48, 51, 102; acceptors, **105**; atom, 7, *8*; cycle, **148**; ion, **41**, **43**, 52, 73, 87, 94, 99, 267, 270, 330; peroxide, **105**, 143; sulphide, **153**, 204.
Hydrogenation, **102**, 105.
Hydrolases, **103**.
Hydrolysis, **46**, 49, 52, 94, 97, **101**, 103, 104.
Hydroxyl ion, **41**, 43, 73, 87, 94, 99, 680; radical, **682**.
Hydrozoa, **671**.
Hypertonic, **82**–85.
Hypocotyl, *438*, 443–*445*.
Hypostome, *185*, **186**.
Hypotonic, **82**–85.

Immunity reactions, 633, **634**.
Inbreeding, **460**, 471, 474, **587**, 588, 613.
Incubation, **405**.
Independent assortment, **470**–*473*–*477*–**478**, 495; law, 458, **478**, 479, 496.
Infra-red, **126**.
Infusoria, **671**.
Ingestion, 75, 108, *109*, 186, 201, 235.
Inhibition, 241, **304**, 317, 320, 341.
Injury, 87, 89; current, **239**, 292.
Insectivora, 651, **674**.
Insectivorous plants, 245, 246, 334.
Insects (*Insecta*), 286, 329, 340, 345, 385, 388, 405, 407, 416, 458, 534, 554, **672**.
Instincts, **339**, 598.
Insulin, 322, **324**, 327, 331.
Intelligence, 320, **344**, 522; tests, 522.
Intercellular substance, *19*, **28**, 34, 39.
Interference, **491**, 495, 496.
Intermediate compounds, **95**, 99; neurones, *255*, **256**.

Intermitotic stage, **354**.
Internal secretion, **275**, 276, **321**.
Internodes, *158*, **159**.
Interracial sterility, 609–614.
Intersexes, **562**; chromosomes, *564*.
Interspecific crosses, 529, 531, 543, 609; hybrids, 529, 615; sterility, **609–614**.
Intestinal glands, 203, *206*; juice, **203**, 205.
Intestine, *187*, 190, *191*, *197*, *200*, 201, 203, 398.
Intracellular canals, **275**; differentiation, 31; membranes, **90**, 265; movements, 259, **273**.
Inversion, 560, **566**.
Iodine, **39**, 222, 327.
Ions, **7**, 9, 41, **42**, 63, 72, 73, 81, 86, 89, 99, 154, 238, 267, 294, 541, 676.
Iris, **289**, *290*.
Iron, **39**, 42, 105, 154, 222; atom, *8*; ions, **42**; sulphate, 122. 136.
Irritability, **240**, 300, 303, 306.
Islands, flora and fauna, 643.
Isolation, **612**; geographical, 604, 612, 643; psychological, **613**; temporal, **613**.
Isotonic, 82–85.

Jimson-weed, *561*.

Ketones, **683**.
Kidneys, 85, 198, 219, **229**, 383, 401.
Kingdom, **36**.

Labyrinth, **285**, 319.
Lactase, **104**, 204, 205.
Lactic acid, 106, **113**, 116, 119, 142, 182, 265–270, 330, 389.
Lactose, **46**, 47, 48, 104, 142, 205.
Lancelets, 649, 673.
Language, **346**; centers, **347**.
Larva, **407**, 418, 529, 631.
Larval structures, 631, 632.
Larynx, **224**.
Latent period, **264**, 270.
Leaf, 160, 163, **167**, *168*, 174, 176, 178, 446, *447*.
Learning, 305, 320, 342, **343**.
Lecithin, 48, **50**, 401, 684.
Lemurs, 634, 652, 674.
Lens, **289**, *290*.
Leucocytes, **210**, 272.
Lichens, **140**.
Life, **3**, 5, **15**, 35, 93, 655, 657; essential characteristics, 658, **662**; nature, **654**, 662, 667; origin, **654**, 660, 663.
Life cycles, *376*, *424*, **440**.
Light, 12, **13**, 14, 122, 154, 176, 279, 541, 593; absorption, *125*, 126, diffraction, 60, 61; dispersion, *125*; reflection, 60; wave length, 125.
Lignin, **167**.
Linkage, **478**; complete, **482**, 487, 496; groups, 479, **495**; incomplete, **483**, 496; laws, **495**.
Lipases, **104**, 111.
Lipins, 46, **48**, 56, 70, 88, 104, 111, 203, 205, 401, 685.
Lipoproteins, **54**.
Liquids, **58**, 64; internal pressure, **64**, 66.
Liver, *197*, 198, *200*, 203, 209, 213, **214**, 219, 234, 398, 400.
Living matter, **5**, 11, 662; origin, 659, 660.
Living things, **3**; simplest, **654**; structure, 16.
Lizards, 421, 624, 651, 673.
Localization, 547–555.
Locus, 488–495, 567.
Long paths, **258**.
Luciferase, **280**.
Luciferin, **280**.
Luminescence, 242, **280**.
Lungs, *197*, 198, *200*, 209, **224**, 398, 401.
Lycopodineae, **670**.
Lymph, 206, **212**; hearts, **212**; nodes, **212**.
Lymphatic tissue, **198**, 211; vessels, 198, *206*, **212**, 401.
Lymphocytes, *210*.
Lysine, **53**.

Macrogamete, **372**.
Macronucleus, 31, *110*, 361, **370**.
Macroscopic, **60**, 62.
Macrosporangia, **432**, *433*, 436.
Macrospores, **432**, *433*, 436, *438*.
Macrosporophyls, **432**, *433*, 435.
Magnesium, **39**, 45, 154, 222; atom, *8*; ion, **42**, 86, 89, 263; salts, 240; sulphate, 122, 136.
Male, **373**.
Maltase, **104**, 204, 205.
Maltose, **46**, 47, 48, 104, 203, 205.
Mammals, 196, 232, 281, 385, 388, 422, **673**; blood relationships, 634; care of young, 406; circulation, *208*, 209; classification, 673; embryonic nutrition, 402–405; geographical distribution, 644–*645*–647; heredity, 519; intelligence, 345; phylogeny, *651*; reproductive organs, 383, *384*; respiration, 224, 225.
Mammary glands, 384, 406.
Man, 184, *200*, 674; behavior, **346**; blood relationships, 634; brain, *309*,

310; chromosomes, 504, 519, *521*; embryo, *633*; heredity, 504, **519**; nutrition, **199**–235; parental care, 406; phylogeny, *652*, 653; reproductive organs, *384*; vestigial organs, 626.
Manganese, **39**.
Map distance, **494**, 514.
Marsupials (*Marsupialia*), 406, 646, 651, **673**.
Mastigophora, **670**.
Maternal inheritance, 526–*527*–530, 542.
Matter, **6**, 107, 155; in living things, **11**; states, **58**; structure, **6**.
Maturation divisions, *409*, **411**–*412*–415, 426, 429, 436, 449, 455.
Mean, **578**, *579*; effects of selection, 581–*582*–*585*–586.
Mechanism, **14**, 15.
Mechano-receptors, **283**, *284*.
Medulla, *308*, *309*, **318**.
Medullary rays, *165*, **166**, *178*.
Medusae, **421**.
Memory, 305, 320, **343**.
Mendel's laws, **458**, 496.
Mental characteristics, inheritance, **522**.
Meristem, *163*, **167**, **442**, 445, 448.
Merostomata, 640.
Mesentery, *196*, **400**.
Mesoderm, 186, *189*, **396**–*397*–*399*–401, 546, 650.
Mesogloea, *185*, **186**, 247.
Mesozoic era, *639*, 640.
Metabolic fragments, **112**; gradients, **549**–552.
Metabolism, **4**, 12, 14, 93, 100, 103, 107, **111**, **179**, 214, **216**, 326, 657; aerobic, **138**; anaerobic, 138, 143; animal, *119*; constructive, 23, 112, **115**, 130, 180, 219, 350; destructive, 23, 42, **112**, 131, 179, 217; embryonic, 401, 549, 550; functional, **24**; green plant, *132*.
Metamorphosis, 328, **407**, 631.
Metaphase, **352**.
Metatheria, **673**.
Metazoa, 184, 380, 392, **671**.
Microgamete, **372**.
Micronucleus, 31, *110*, 361, 370.
Micropyle, **386**, **437**.
Microscopic, **60**, 62.
Microsporangia, **432**, *433*, 436.
Microspores, 432, *433*, 436, *438*.
Microsporophyls, **432**, *433*, 435.
Midbrain, *308*, *309*.
Milk, 48, 54, **406**.
Mimosa, 245, 334.
Mirabilis, 459, 510.
Mitosis, **351**, *352*, *353*, 361, 455, 531; evolution, 665; in simple organisms, 358; mechanism, **357**; significance, **354**.
Mixed population (*see* Populations).
Mixotrophic, **145**.
Mixture, **6**, 7, 11, 38, 98.
Mode, **578**.
Modifications, 557, **573**; inheritance, 574, 604, 615, 617.
Molds, *137*.
Molecules, **6**, 12, 44, 75–92; attractions, 13, 64–67, 71; formulas, **675**; orientation, 66–*68*, 90; size, 58, 61–63; structure, **9**, *10*.
Molluscoida, **672**.
Molluscs (*Mollusca*), 256, 279, 345, 421, **672**; phylogeny, *648*.
Monkeys, 346, 634, 652, 674.
Monocotyledons (*Monocotyledoneae*), *164*, 165, 443, **670**.
Monoecious, **373**, 380, 382.
Monosaccharoses, **46**, 47, 101, 106.
Monotremes (*Monotremata*), 402, 646, 651, **673**.
Morgan's laws, **495**.
Morphogenesis, **349**.
Mosaics, **532**, *533*, 555, 565, 571.
Moss, **160**, *161*, 670; nutrition, 160, 183; reproduction, **427**, *428*, 441.
Mouth, 184, 187, 189, 201; development, 395, *397*, *399*, 400.
Movement, 3, 4, 14, **259**.
Mucin, **202**.
Mucor, *137*, 669.
Mucus, **202**.
Multicellular organisms, 16, 28, **34**; origin, 655, 665.
Multiplication, **349**, **590**, *591*, *592*.
Musci, **670**.
Muscle, *188*, *190*, *196*, 216, 251, 252, 257, **259**, 398; cardiac, *260*, **261**–263, 298; cells, 26, 251, 254, *260*; fibers, *260*, **261**; involuntary, **262**; processes, 185, **247**, *248*, 299; skeletal, *260*, **261**–264; smooth, **260**–263; spindle, *284*; striated, **262**; tissue, 187, 189, 199, 251, *260*; twitch, **264**; visceral, **262**, 298; voluntary, **262**.
Muscular movement, 259, **264**.
Mutation, 514, 515, 557, **567**, 589, 598, 602, 607, 608, 616, 627, 629, 658, 660, **662**.
Mycelium, **136**.
Myelin sheath, **309**, 313.
Myofibrils, **247**, *248*, **259**, 261, 267–270.
Myonemes, *244*, **245**, 259.
Myo-neural junction, **254**, 301, 305.
Myriapoda, **672**.

Narcotics, **240**.
Natural selection, 590, **595**, *606*, 664, 666; and modern genetics, **614**; limitations, 600; objections, 616.
Nearctic region, *645*, 646.
Nemathelminthes, 648, 650, **671**.
Nematodes (*Nematoda*), 503, **671**.
Nemertinea, **671**.
Neotropical region, *645*, 646.
Nephridia, *190*, *194*, **195**.
Nerve cells, 26, 185, *248*, 249, **253**, *254*, **295**, 305; centers, **318**; cord, *188*, *190*, *196*, *253*; fibers, *248*, 249, **253**, **295**, 306, 313; impulse, 242, **293**, *295*; net, 249, **299**, 312; tissue, 199, **252**, 299.
Nerves, 35, *190*, **253**, **312**, 401.
Nervous system, 35, 187, 249, 252, *253*, *308*, 332, 398; central, **252**, 300, **307**; conduction paths, **314**, *315*, 348; diffuse, **249**; fiber tracts, 316; synaptic, **300**.
Nettle-cells, 185, *248*.
Neural folds, **398**, *399*, 546; groove, 398, 546; tube, **398**, *399*, *548*.
Neuroid transmission, **298**.
Neurones, **253**, *254*, 305; intermediate, *255*, **256**, *257*, 258, 309, 319; motor, **254**, *255*, *257*, 309, 310; sensory, **253**, *255*, *257*, 282, 310.
Neutral, **681**.
Neutrality, maintenance, **43**, 228.
Neutralization, 266, 270, **680**.
Nitella, **157**, *158*, 183, 273, 669.
Nitrate, 128, 139, 144, 149, 150; bacteria, **150**; ion, **42**.
Nitrite, 128, 144, 150; bacteria, **150**; ion, **42**.
Nitrobacter, *151*.
Nitrogen, 11, **39**, 40, 42, 45, 48, 51, 128; atom, *8*; cycle, **149**; fixation, **151**–153; free, **149**–151.
Nitrosomonas, *151*.
Nodes, *158*, **159**.
Non-disjunction, 559, **563**.
Non-electrolytes, **63**, 70, 81.
Nonpolar compounds, **10**, 48, 66, 77, 86, 88; radicals, 45, 66.
Normal curve, **578**, *579*, 581.
Notharctus, 652.
Notochord, *399*, **400**, 546.
Nuclear membrane, **19**, *20*, 27, 90, 351, 355, 357, 665; sap, **20**, 414.
Nucleic acid, **54**, 115, 117, 130, 215, **518**, 684.
Nucleolus, *20*, **22**, 357.
Nucleoplasm, **20**, 90, 355.
Nucleoproteins, **54**, 55, 402, **512**, 516, 635, 656.
Nucleus, 4, 16, 19, **20**, *23*, 306, 352, 386, 516, 655, 665.
Nutrition, **3**, **4**, **107**; animal, **108**, *121*, 134, 184, *199*; atypical modes, **135**; autotrophic, **144**; embryonic, **401**; evolution, 666; green plant, **122**, *134*, 156, *169*; heterotrophic, **145**; holophytic, **122**, 134, 144; holozoic, **108**, 134, 145; mixotrophic, **145**; modes, **144**; saprophytic, 137, 145.

Oedogonium, *425*, 426, 441, 669.
Oils, 11, 48, 67–69.
Oleic acid, **49**.
Olfactory cells, *289*; lobe, *308*, *309*.
One-factor cross, 458–**460**–*461*–*466*–470, 518.
One-way conductivity, **301**.
Ontogeny, **632**.
Onychophora, **672**.
Oocytes, **411**, 414, 488, 527, 550.
Oogonia, **410**, 527, 554.
Ophiuroidea, **672**.
Order, **37**.
Organic acids, 63, 106, **683**; bases, 50, 63, 106, 115, 130, 215, **684**; compounds, 3, 11, 15, 40, **44**, 55, 102, 664, **680**, **681**; salts, 45, 63, **683**.
Organism, **4**, **28**, 35; a physico-chemical mechanism, 15.
Organizers, **548**–555.
Organogeny, **398**.
Organs, **35**, 162, **184**, 186, 398; systems, **35**.
Oriental region, *645*, 647.
Origin of species, **602**, *606*, 618.
Orthogenesis, **617**.
Oscillatoria, *359*.
Osmosis, **78**, *79*, 91, 111, 172, 205, 233, 404.
Osmotic pressure, **80**, 173, 277, 291, 525, 541; work, 234.
Outcrossing, **588**.
Ovaries (of animals), **380**, *381*, *383*, *384*.
Ovary (of flower), *435*, **436**, 439.
Oviducts, **382**, *383*, *384*, 402.
Oviparous, **389**; mammals, 402.
Ovule, *435*, **436**; integuments, 437.
Ovum, **373** (*see* Egg-cell).
Oxalic acid, 182, **683**.
Oxidases, **103**.
Oxidation, 15, 24, **101**, 104, 112, 148, 179, 218, 240, 268, 278, 296, 326, 402.
Oxygen, 11, **39**, 41, 45, 46, 48, 51, 101, 105; atom, *8*; consumption by muscle, 264–270; consumption by nerve, 296; cycle, **148**; effects on development, 525, 540; free, *7*, 15, 40, **42**, 108, 133, 148, 154; liberation by photosynthesis, 127, 148,

177; respiration, 119, 132, 180, 193, **225**; solubility, 120, **226**; transportation, 194, **226**.
Oxygenation, **102**.
Oxyhemoglobin, **226–228**.

Pacinian corpuscle, *284*.
Pain, **292**.
Palearctic region, *645*, 646.
Paleontology, **637**.
Paleozoic era, 638, *639*, 640.
Palmitic acid, **49**, 679.
Pancreas, *197*, 198, *200*, 203, **322**, 324, 398, 400.
Pancreatic juice, **203**, 205.
Pandorina, 367, *372*.
Parahormones, **330**.
Paramecium, 31, 108, *110*, 121, 671; galvanotropism, *337*; motor reflex, *334*, 338; reproduction, 361, 370, 375.
Parasites, 139, **140**, 541, 594.
Parasitism, **140**.
Parasympathetic system, **310**, *311*.
Parathyroid glands, 327; hormone, 322, **327**.
Parenchyma, *161*, **162**, *165*, 166, 167, 178, **187**, *188*.
Parental care, **405**.
Parthenogenesis, **415**, *417*, 449, 504, 508; artificial, **418**; diploid, **416**; haploid, **416**, 563.
Peas, 439, 444; heredity, 465, 470.
Pedogenesis, **418**.
Pelargonium, 511.
Pelecypoda, **672**.
Pellicle, 28, *110*.
Pepsin, 99, **104**, 203–205.
Peptide linkage, **52–54**.
Peptones, **55**, 104, 203–205.
Peristalsis, **202**.
Peritoneum, **189**, *190*, *196*.
Permeability, 77, **85**, *88*; changes, **86**, 239, 240, 245, 265, 277, 278, 389.
Petals, **434**, *435*.
Petiole, **167**.
Phaeophyceae, **670**.
Phagocytosis, **272**, 407, 408.
Pharynx, *187*, 190, *197*, *200*, **201**, 202, 223, 400.
Phase, 64, 72; boundary, 67, *68*, 90, 91; continuous, 68, 76, *88*; dispersed, 68, 76, *88*; reversal, **69**, 73, 89.
Phenotype, **470**, 475, 558.
Phloem, *163*, *165*, **166**, *168*, 178, 446, *447*.
Phoronida, **672**.
Phosphate, 43, 99, 130, 153, 171, 229, 231; ions, **42**, 43, **681**; radical, 45, 54, 153, **685**.
Phospholipins, 48, **50**, 51, 56, 63, 67, 70–72, **89**, **203**, **213**, **219**; synthesis, 117, 130.
Phosphoproteins, **54**, 117.
Phosphoric acid, **681**.
Phosphorus, **39**, 42, 45, 48, 51, **222**; atom, *8*; cycle, **153**.
Photo-chemical reactions, **288**.
Photo-receptors, 245, **288**.
Photosynthesis, 15, **125**, *134*, 148, 159, 160, *169*, **176**, 183; efficiency, 176; rate, 177.
Phototropism, **336**, *337*, *338*, 340, 444.
Phycomycetes, **669**.
Phylogeny, 632, **647**, *648*, *651*, *652*.
Phylum, **36**.
Physico-chemical mechanism, **15**.
Pigments, 25, 87, 131.
Pineal gland, 322, 330.
Pistil, **435**, 436.
Pith, *163*, *165*, **166**, 178, **446**, *447*.
Pithecanthropus, 652.
Pituitary gland, 324, 328, 535.
Pituitrin, 322, **324**, 325, 327.
Placenta, *403*, **404**, 406.
Planaria, **186**, *187*, *188*, 235, 671.
Plants (*Plantae*), 30, 36, **669**; nutrition, 122–145, 156–183; reproduction, 423–451; responsive mechanisms, **245**.
Plasma membrane, **27**, 90; permeability, 77, 78, 81, **88**, 172, 228, 238, 239, 245; polarization, **238**; structure, 73, **87**, *88*.
Plasmodium, *32*.
Plasmolysis, *82*, 83.
Plastids, *18*, **25**, 31, 73, 91, 101, 357; inheritance, 509–512.
Platyhelminthes, 648, **671**.
Pleodorina, 367, *368*, 372.
Pleurococcus, *31*, 33, 364, 369, 669.
Polar bodies, *409*, **415**, 544, 545.
Polar compounds, **9**, *10*, 40, 65, 66, 77, 86, 88; radicals, 45, 66
Polarity, **545**.
Polar-nonpolar compounds, *10*, **11**, 66, 70, 71.
Pole, **544**–*547*–551.
Pole cells, **396**, *397*.
Pollen grains, *435*, **436**, *438*, 511, 530; sacs, 436; tube, *435*, **437**, 511, 530.
Pollination, 437.
Polyembryony, **419**, 508.
Polypeptides, **53**, **54**.
Polysaccharoses, **46**, 47, 63, 70, 72, 85, 94, 101.
Polyzoa, **672**.
Pons, *309*, *315*.
Populations, growth, *591*, *592*, *593*; limitation, **591**; mixed, 576, **581**, 584, 587.

Porifera, 648, **671**.
Portal vein, *208*, **209**, **213**.
Potassium, **39**, 154, **222**; atom, *8*; bicarbonate, 128, **227**; chloride, **228**; hydroxide, 49; ion, **42**, 51, 71, 86, 89, **228**, **240**, **263**; nitrate, 122, 128, 150; nitrite, 128, 150; phosphate, 136.
Potential difference, **238**.
Precipitation test, **634**.
Primates, 346, **674**; phylogeny, *651*, *652*, 653.
Primordial germ cells, *409*, **410**.
Probability curve, **578**.
Prophases, **352**, 391.
Propliopithecus, 652.
Proprioceptors, **285**, 319, 320.
Prosopygia, 648, 650, **672**.
Proteases, **104**, 111.
Proteins, 3, 46, **51**, 56, 66, 67, 85, 89, 104, 108, 685; as antigens, 634; conjugated, **54**, 117, 130; digestion, 111, **203–205**; dispersions, 63, 70–72; fuel value, 115, 218; in enzymes, 99; in genes, 513; ions, 52, 70, 71, 81, **267**; metabolism, 114–116, 214, **219–221**; osmotic pressure, 81; rôle in muscular movement, **266–270**; simple, **54**; size of molecules, *17*, 58, 61, 63; specificity, 54, 633; stored, 179, 401; synthesis, 116, 130, 177, 221.
Protenor, chromosomes, *499*.
Proteoses, **55**, 104.
Proterozoic era, 638, *639*, 640.
Prothallium, **430**, *431*, 432, *433*, **441**.
Protonema, *428*, **429**, 441.
Protoneurones, **299**.
Protons, 6, 7.
Protoplasm, **3–5**; activities, **4**; appearance, **73**; composition, 3, 11, 38, **56**; consistency (viscosity), **59**, 69, 73; constituents, **39**; neutrality, **43**; physical state, **58**; structure, 3, 12, 58, **72**; *73*, 90.
Prototheria, **673**.
Protozoa, 31, 33, **36**, 184, 665, **670**; cell division, 358–361, 508; heredity, 509; nutrition, **108**–*121*, 235; phylogeny, *648*, 649; reproduction, 362–379; responsive mechanisms, 244.
Pseudopodia, *30*, *109*, 186, 244, **272**.
Pteridophytes (*Pteridophyta*), 162, **670**; growth, 442; phylogeny, *648*, 649; reproduction, 423, **430**, *431*, *433*, 449–451; stem, *164*, 165.
Ptomaines, **142**.
Ptyalin, 98, 99, **202**, 205.
Pulmonary arteries, *208*, **209**; veins, *208*, **209**.
Pupa, **408**, 531.
Pupil, **289**, *290*.
Pure lines, *582*, **583–587**, 613.
Putrefaction, **142**.
Pylorus, **203**.
Pyrenoid bodies, *33*, *123*, 127, *141*.
Pyruvic acid, **113**; aldehyde, **113**.

Radicals, **11**, 44, **675**, 679, 681.
Radicle, *438*, *443*, **444**, *445*.
Ranatra, *337*.
Reason, **347**.
Recapitulation, **632**, 633.
Receptacle, *435*, **448**.
Receptive substance, **301**.
Receptor-conductor-effector system, **250**.
Receptor-effector system, **249**, *250*.
Receptors, **243**, 249, 252, 258, **282**.
Recessive, **465**, *466*–470, 475, 479, 482, 532, 568, 587.
Recombinations, 470, 482, 487, 490, **557**, 586, 597, 615; percentage, 488, 495, 496.
Recovery, 87; period, **264**, 268, 270; process, **269**, 273, 276, 296.
Rectum, *200*, 201, 206; development, *399*.
Red blood corpuscles, **210**, 226–228; crenation, *83*; cytolysis, 84; size, *17*.
Reduction (chemical), **101**, **102**, 105, 116, 128, 130, 138.
Reduction division, **374**, *375*, **411**, *412*, 423, 429, 441, 449, 455, *456*, 460, 464, 472, *473*, *477*, 478, 530.
Reflex action, **333**; arcs, **255**, *257*, 301, *315*, **316**, **317**, 333; time, **302**.
Reflexes, **255**, **333**; compound, **339**; conditioned, **343**; intersegmental, **256**; segmental, **256**.
Refractory period, **240**, *295*, *297*, 299; absolute, **297**; relative, **297**.
Regeneration, **421**, 450.
Relaxation period, **264**, 270.
Reproduction, 3, 5, 349, 350, **362**, 516, 661; asexual, **362**, 415, 423, 507, 584; sexual, **362**, **369**, 377; 380, 423; vegetative, **450**.
Reproductive organs, 187, 328, **380**, *381*, *383*, *384*, 398, 427, *428*, 430, *431*, *433*, *435*.
Reptiles, 196, 209, 215, 232, 345, 383, 388, 402–405, 422, 635, 651, **673**.
Respiration, **120**, 132, 180, 183, 186, 188, 193, **223**, 235.
Respiratory center, 306, 318, 330; organs, **193**, 198, **223**.
Response, **237**, **242**; electrical, **238**, *264*, 265, 270, 278, 280, 389; local-

ization, **302**; mechanical, **242**, *264*, 265; modifiability, **303**.
Responsive mechanisms, **244**.
Responsiveness, 3, 4, **236**, 333.
Resting spores, **366**, 378; stage, **19**, 20, 30, 351, 358.
Retina, **289**, *290*, *291*.
Reversible reactions, **96**, 100, 102, 106, 114–118, 127, 214; equations, **679**.
Rhizopods (*Rhizopoda*), 369, 430, **670**.
Rhizoids, *157*, *158*, 159, 160, *161*, 162, 430.
Rhodophyceae, **670**.
Rodentia, 651, **674**.
Rods, **289**, *291*.
Root, **163**, **167**, 170, 178, 182, *246*, 336, 444–*447*; cap, *447*, 448; hairs, *23*, 167, **170**, *171*, 172, 444, 448; nodules, *152*; pressure, **173**.
Roses, chromosomes, *562*.
Rotifers (*Rotifera*), 416–418, 505, **671**.
Roundworms, 418, 671.

Saccharases, **104**.
Saccule, **285**, *286*.
Salamanders, 421, 651, 673.
Saliva, 97, 202, 205.
Salivary glands, 198, *200*, 202.
Salts, 10, 40, **41**, 45, 56, 63, 81, 86, 108, 111, 117, 122, 128, 154, 170, 172, 177, 221, 229, 231, **680**.
Sap, **172**; ascent, **172**.
Saponification, **49**, 50, 51.
Saprophytes, **139**.
Saprophytic, **137**, 145; bacteria, **142**.
Sarcodina, **670**.
Sarcoplasm, **259**, 261, 267, 270.
Scaphopoda, **672**.
Schizomycetes, **669**.
Schizophyceae, **669**.
Schizophytes (*Schizophyta*), **36**, 665, **669**; age, 640; phylogeny, *648*, 649; reproduction, 369, 376, 378.
Scleroproteins, **54**, 55.
Scyphozoa, **671**.
Sea-urchins, 529, 672.
Seaweeds, 34, 159.
Secondary sexual characters, 328, 384, 534.
Secretin, **322**.
Secretion, 27, **91**, 242, **274**; internal, **321**; mechanism, **276**, *278*.
Secretory granules, 26, 275, 277.
Sedimentary rocks, **636**, 637, 640.
Seed, 434, **437**, *438*, 444, *445*; coats, **437**, *438*, 444, *445*.
Seed-plants, 162, 423, 434, 443, 451, 458, 503, 529, 670.
Segregation, 458–**464**–469, 496, 512; law, 458, **464**, 469, 486, 496, 512.
Selaginella, **432**, *433*, 441, 670.
Selection, **580**, *582*, *585*; artificial, compared with natural, 590, 596, 601.
Self-differentiation, **549**; -fertilization, **387**, 581–584, 613; -pollination, **437**, 581.
Semicircular canals, **285**, *286*.
Seminal fluid, **382**; vesicles, **382**, *384*.
Semi-permeable membranes, **77**–*79*–81.
Sensation, **283**, 319.
Sense organs, 258, 282–292; development, 398, 401, 546.
Sensitive plant, 245, 246, 273, 334.
Sensory cells, 185, *248*, **249**, 252, 299; ganglia, *257*, 258, **310**, *312*, 313; neurones, **253**, *255*, *257*, 258, 310.
Sepals, **434**, *435*.
Septa, 189, *191*, *194*, 396, *397*.
Sex, 373; chromosomes, *497*, **498**, *499*, *506*, *521*; determination, 496–507, 535, 563; hormones, 322, **328**, 535; inheritance, **496**; linkage, *500*, **502**–505, 521, 564.
Sharks, 331, 673; embryo, *633*; gills, *224*.
Sieve-tubes, *165*, **167**, 168, 178, 245, 298.
Silicon, **39**, 222; atom, *8*.
Silkworm, 526.
Sirenia, 651, **674**.
Skeletal materials, 39, 42, 54, 55, 107.
Skeleton, 196, 398, 400, *624*, 641, 650.
Slime molds, *32*, 670.
Smell, 287, 288; receptors, 287, *289*.
Snails, 345, 528, 672.
Snakes, 651, 673.
Soaps, **49**, 66–*68*, 203, 213.
Sodium, **39**, 154, 222; atom, *8*; bicarbonate, 194, 211, 227, 228, **681**; carbonate, 203, **681**; chloride, *10*, 211, 222, 228, 231; hydroxide, 49; ion, **42**, 68, 86, 89, 228, 240, 263, 327.
Soil, 149–152, *171*, 182.
Solids, 58, **59**, 71, 89; porous, **76**.
Solubility, 11, 40, 45, 66.
Solute, **62**.
Solutions, 60, **62**, 66, 70, 72, 75–92.
Solvation, **60**.
Solvent, **62**.
Soma, **453**, 454.
Somatic cells, **367**, *368*, 408, 452.
Species, **37**, **609**; hybrids, **609**; origin, 602.
Spectrum, **125**; absorption, of chlorophyl, *125*.

Sperm nuclei, **437**, *438*; receptacles, **382**, 388.
Spermaries, **380**, *381*, *383*, *384*.
Spermatids, *409*, **414**.
Spermatocytes, **410**, 414.
Spermatogonia, **410**.
Spermatophytes (*Spermatophyta*), 162, **670**; growth and development, **442–448**; phylogeny, *648*, 649; reproduction, 423, **434**, 449–451.
Spermatozoon, **373** (*see* Sperm-cell).
Sperm-cell, *372*, **373**, 381, 386, *387*, **414**, 427, *428*, 430, *431*, *433*, 512.
Spermiducts, **382**, *383*, *384*.
Sphaerella, 367.
Sphaerocarpos, sex-chromosomes, *506*.
Spinal cord, **307**, *308*, *312*, *399*, 400; nerves, *312*, **313**.
Spindle, 352, 358; fibers, 352, 354, 358.
Spirilla, *142*.
Spirogyra, *33*, 34, *61*, 84, 669; reproduction, 364, *369*, *375*, 441.
Sponges, 298, 396, 397, 420, 421, 671.
Sporangia, **430**, *431*, 432, *433*.
Spores, 32, **365**, *371*, 376–378, 423–*425–428–431–433*–441, 449, 505.
Sporocytes, **426**, 429, 436.
Sporophyls, **430**, 432, *433*.
Sporophyte, **376**, 423–*428–431–433*–441, 449, 450, 505.
Sporozoa, **670**.
Stamens, **435**, 440.
Standard deviation, *579*; effects of selection, *582*, *585*.
Starch, 25, **46**–*48*, 97, 104; digestion, 202, 203, 205; storage, 127, 178; synthesis, 127, 177, 530, 536.
Starfish, 345, 672; development, *393*–395.
Starvation, 118, 214, 219.
Statistical methods, **576**, 580.
Statistics, **578**, *579*.
Statocyst, **285**.
Statolith, **285**.
Steapsin, **203**, 205.
Stem, **163**, **164**, *165*, 172, 336, 445–*447*.
Stereotropism, **336**, 337.
Sterols, 48, **51**, 56, 117, 130.
Stigma, *435*, **436**, 437.
Stimuli, **237**, **241**, 282, 306; combinations, 341; negative, 343; repetition, 341; substitution, 343, 344; summation, **303–304**, 342.
Stomach, *197*, *200*, 201, **202**, 398.
Stomata, 166, *168*, **169**, **174**, *175*.
Stored food substances, 38, 47, 51, 55, 115–118, 127, 130, 138, 178, 214, 216, 219.
Structural characters, **623**.
Struggle for existence, **594**.
Style, *435*, **436**.
Substance, **6**.
Substrate, **99**.
Sucrase, 99, **104**, 137, 204, 205.
Sucrose, 46, **47**, 48, 94, 104, 136, **137**, 179, 204.
Sugars, 45, **46**, 63, 81, 86, 173.
Sulphate, 115, 120, 130, 153, **229**, **231**; ion, **42**.
Sulphur, **39**, 42, 45, 51, 115, 130; atom, *8*; bacteria, 144, *153*; cycle, **153**; free, 153.
Summation (*see* Stimuli).
Sun, 15, 154, 155.
Sundews, 245.
Supernormal period, **297**, 304, 344.
Surface film, **64**, 72, 90; tension, **41**, **64**, *65*, **66**, 272.
Surface-active substances, **66**, 90.
Survival of the fittest, **595**.
Suspensions, **60**, **63**.
Swarm-spores, **365**.
Sweat glands, 234, 281.
Symbiosis, **140**, 152.
Symbols, chemical, **675**.
Sympathetic system, **310**, *311*, **323**.
Synapse, 254, *255*, **301**–305.
Synapsis, **411**, *412*, 425, 449, 457, 483–491.
Synaptic block, **301**; fatigue, **304**; nervous system, **300**.
Syncytia, **22**, **31**, *32*, 136, *137*, 159, 261, 262, 299, 355.
Synthesis, 97, 103, 112, 115, 128, 130, 144, 177, 180, 219–221, 276, 349, **350**; dehydrolytic (dehydration), 47, 49, 52, **101**, 103, 115–117.

Tactile corpuscle, *284*; receptors, **283**.
Taste, 286, 288; buds, **287**, *288*.
Teleostomi, **673**.
Teleosts, 651, 673.
Telolecithal eggs, **385**, *386*, 394.
Telophases, **353**, 354.
Temperature, **62**, 76; coefficient, **96**; effects on chemical reactions, **95**–100; effects on development, 525, 536, **539**; effects on mutation, **572**; regulation in warm-blooded animals, 218, **281**, 291, 306, 318.
Tendons, 198, **261**, *284*.
Testes, **380**, *383*, *384*.
Tetanus, **263**.
Tetrads, *412*, **413**.
Tetraploid, **560**, *561*, *562*.
Thalamus, *308*, *309*, 318.
Thallophytes (*Thallophyta*), **36**, 665, **669**; cell division, 360; growth, **442**; phylogeny, *648*, 649; reproduction, 369, 423, **424**.

Thermo-receptors, 281, **291**.
Thinking, **347**.
Thiospirillum, *153*.
Thirst, 291.
Three-factor cross, 477.
Thymus gland, 322, 329.
Thyroid gland, **326**, 535.
Thyroxin, 322, 325, **326**, 327.
Tissues, **34**, 162, 164, 184, 185, 186, 188, 198, 397, 446; systems, *163*, **164**.
Tonus, **263**.
Touch, 283.
Trachea, *200*, **224**.
Tracheids, **167**, 168.
Translocation, 560, **566**.
Transpiration, 172, 173, **174**.
Transplantation, 547, *548*, 551, 555.
Trematoda, **671**.
Trilobita, 640.
Tripalmitin, **49**.
Triploid, 437, **560**, *561*, *562*, 563, *564*.
Tropisms, **335**, 598.
Trypsin, 99, **104**, 203–205.
Tryptophane, **53**.
Tube nucleus, **437**, *438*, *439*.
Tubers, 178, **451**, 584.
Tunicates (*Tunicata*), 420, **421**, 650, **673**.
Turbellaria, **671**.
Turgor, 26, **85**, 87, 174; movements, 245–247, 259, **273**.
Turtles, 651, 673.
Twins, fraternal, 508; identical, **419**, 508, 522; Siamese, 420.
Two-factor cross, **470**, *476*.
Tyrosine, **53**, **324**, 326.

Ulothrix, *157*, 669; reproduction, *366*, *371*, 377.
Ultramicroscope, **60**.
Ultramicroscopic organisms, 17, **28**, **657**; particles, **61**, 62; pores, 76, 77.
Ultra-violet, **126**, 553.
Umbilical cord, **404**.
Ungulata, 651, **674**.
Unicellular animals, **108**; green plants, **122**; organisms, 16, 28, **30**; 655, 665.
Univalents, **411**, 412, 486.
Urea, **115**, 120, 149, 215, 229, 231, 331, **685**.
Urease, 99, **115**.
Ureter, *197*, *200*, *229*, **230**, *383*, *384*, 401.
Urethra, *200*, **230**, 383, *384*.
Uric acid, 115, 120, 150, 215, 229, 231.
Urinary bladder, *197*, *200*, 230, *384*, 398, 401, 404; tubules, **229**, *230*, 401.
Urine, **230**; production, 231–234.
Urino-genital system, **383**.
Urochorda, 650, 651, **673**.
Uterus, **382**, *383*, *384*, 402–404.
Utricle, **285**, *286*.

Vacuolar membranes, 27, 73, 88, **90**.
Vacuoles, *18*, 24, **26**, *33*, *82*, *123*, 276, 355; contractile, 27, *30*, *110*, **120**, *141*; food, *30*, **109**, *110*.
Vagus nerves, 311, 314.
Variability, 379; effects of selection, 581–*582*–*585*–587; measurement, 578.
Variation, **557**, 595, 614–618; continuous, 559, **575**; discontinuous, **576**; genetic, 557, 586, 595, 604, 615.
Varieties, **609**.
Vascular plants, **162**; nutrition, **169**–183.
Vaucheria, *32*, 669.
Veins, *206*, **207**, *208*, 209, 213.
Ventricles, **207**, *208*, 209.
Venus flytrap, 245.
Vermiform appendix, *200*, 626, 628.
Vertebrae, *196*, *197*, *200*, 400.
Vertebrates (*Vertebrata*), **195**, *196*, **673**; development, 395, 396, **398**, *399*; embryos, *633*; fossils, 641; gill-slits, 632; hormones, 322, 535; limbs, *624*, 625; nervous system, **307**; nutrition, **199**, 235; phylogeny, 649–*651*; regeneration, **421**; reproductive organs, 382; responsive mechanisms, 256, *257*; secondary sexual characters, 385, 534.
Vestigial organs, **626**; embryonic, 633.
Viability, 518, 598.
Vigor, 378, **587**.
Villi, intestinal, **205**, *206*, 213; placental, 404.
Viscosity, 41, 59, 69, 70, 72, 76.
Visibility of particles, **60**.
Visual purple, **289**.
Vitamines, **222**.
Vitelline membrane, **385**, *386*.
Viviparous, **389**.
Volvocaceae, 367, *368*, 371, *372*.
Volvox, 367, *368*, 372, 669; gametes, *372*.
Vorticella, *244*, 335, 671.

Wallace's line, *645*, 646.
Warm-blooded animals, 14, 49, 217, 281, 306.
Wasps, 345, 405, 416, 505.
Waste products, 39, 42, 91.
Water, **40**, 56, 59, 65, 77, 86, 102, 103, 108, 113, 120, 122, 124, 176, 221, 229, 231, 277, 292, 540, 593, 680; molecule, *10*.

Wood, **166**, 446; fibers, *165*, **167**, 446.
Workers, **405**.

X-chromosome, *497*, **498**, *499*, *506*, *521*, 534, 562, *564*.
X-rays, 12, **13**, 486, 567, 572.
Xylem, *163*, *165*, **166**, *168*, 172, 178, 446, *447*.

Y-chromosome, *497*, **498**, *506*, *521*, 562, *564*.
Yeast, 33, *135*, 325, 670; budding, *364*; nutrition, **136**; rate of multiplication, *591*, 592; spore formation, *365*.
Yolk, **385**, *386*, 394, 401, 411, 545, 552; cells, *399*; plug, *399*, *547*; sac, *403*.

Zinc, **39**.
Zone of elongation, **445**.
Zoo-geographical regions, 644, *645*.
Zooids, **421**.
Zoospores, **366**, 371.
Zygospore, *369*, **370**, 371, 374, *375*, 378.
Zygote, **369**, *371*, *375*, *390*, 391, 392, 408, *425*, 525, 530.

V
O
O
P
CT
S
T
A
SH
CA

CANCELLED

CANCELLED